# The Journal of Obstetrics and Gynaecology of the British Empire

Issued under the Direction of the Royal College of Obstetricians and Gynaecologists

EDITOR

JAMES YOUNG

EDITORIAL REFERENCE COMMITTEE

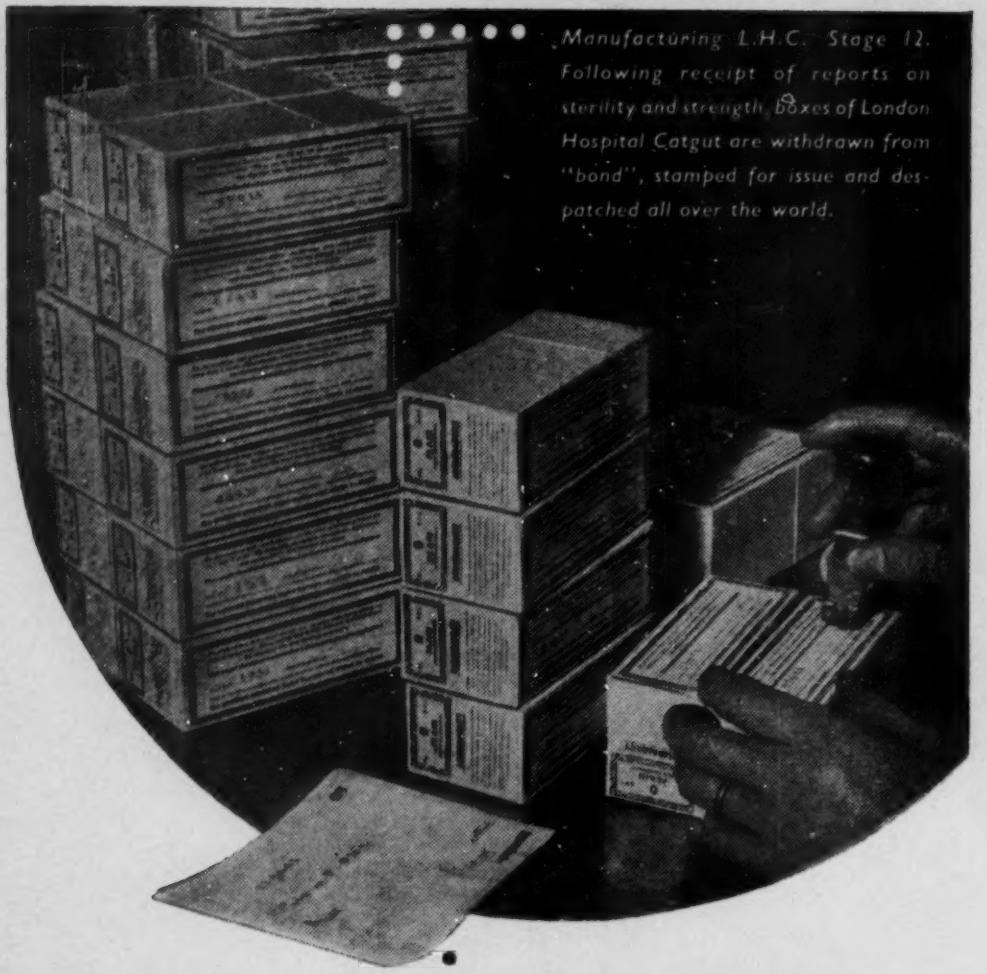
DUGALD BAIRD J. C. McCLURE BROWNE

S. G. CLAYTON

VOL. LX, NO. 6 DECEMBER 1953 PRICE 12*s.* 6*d.* NET

*Entered as Second Class at the New York, U.S.A., Post Office*

JOHN SHERRATT AND SON, *PUBLISHERS*
ALTRINCHAM, ENGLAND



*Manufacturing L.H.C. Stage 12. Following receipt of reports on sterility and strength, boxes of London Hospital Catgut are withdrawn from "bond", stamped for issue and despatched all over the world.*

**London Hospital Catgut**
**is manufactured under unified control from intestine to sterile tube**

*Specify* LHC

OBTAINABLE FROM ALL LEADING SURGICAL EQUIPMENT HOUSES

WHG12

*Sublingual Therapy with*

STEROID HORMONE

# 'LINGUETS'

**Maximum effectiveness and economy**

**PERANDREN** *
(Methyltestosterone B.P.)

**ETICYCLIN** *
(Ethinyloestradiol B.P.)

**OVOCYCLIN** *
(Oestradiol B.P.C.)

**LUTOCYCLIN** *
(Ethisterone B.P.)

**PROTANDREN** *
(Methylandrostenediol)

**FEMANDREN** *
(Methyltestosterone B.P.
and Ethinyloestradiol B.P.)

**CIBA hormone 'Linguets'* are available in a range of strengths and packages.**

'Linguets' cost no more than B.P. Tablets.

CIBA

* *Registered trade marks. Reg. user*

**CIBA LABORATORIES LIMITED**

HORSHAM · SUSSEX

*Telephone: Horsham 1233* *Telegrams: Cibalabs, Horsham*

4/3

*Containers of 250 c.c., 500 c.c. Ampoules of 6 c.c. in containers of 5 and 25.*

*in obstetrics*

'Trilene' analgesia in labour is both pleasant and effective. The drug is equally safe for mother and child, and there are no contra-indications. Recovery is rapid, with no unpleasant after-effects. With these notable characteristics, 'Trilene' has achieved a widespread reputation among obstetricians as a most valuable analgesic.

**'TRILENE'**
TRADE MARK (Trichloroethylene)

IMPERIAL CHEMICAL (PHARMACEUTICALS) LIMITED
*A subsidiary company of Imperial Chemical Industries Limited*
WILMSLOW, MANCHESTER

Ph.415

ICI

# Operative Gynecology

**By Richard W. Te Linde**

*Professor of Gynecology, Johns Hopkins University and Chief Gynecologist, Johns Hopkins Hospital*

THIS is the Second Edition, and the first English edition, of an American book by an authority with experience in the practice and teaching of gynecology gained over a period of twenty-five years. Already considered to be a classic in its field, this exhaustive work has been written with the primary purpose of describing the technique of the usual (and some of the rarer) operative procedures. It includes indications for and against operations, as well as pre- and post-operative care of patients. Some consideration is also given to such matters as gross and microscopic pathology, and psychology and psychiatry in relation to gynecology.

For this second Edition, new material has been added covering the recent great advances in the subject, and over 100 new illustrations have been included.

Pages 907+xxiv. 7 in. by 10¼ in. £6 net

**PITMAN**
**Parker St., Kingsway, London W.C.2**

# VERILOID*

## INTRAMUSCULAR SOLUTION *in* PRE-ECLAMPSIA

### Prompt Relief of Symptoms and Rapid Control of HYPERTENSION

Veriloid Intramuscular Solution offers a positive and dependable means of rapidly reducing the blood pressure, and so maintaining it for prolonged periods if necessary. A single dose of this hypotensive extract of Veratrum viride produces its maximum effect in 60 to 90 minutes. In most patients blood pressure can be controlled by injections repeated every three to six hours. Thus, when the arterial tension must be depressed for hours or days, Veriloid Intramuscular Solution can accomplish this therapeutic objective.

*A buffered, aqueous, isotonic solution containing 1.0 mg. of standardized Veratrum viride alkaloids per cc., together with 1% of procaine hydrochloride. Packaged in boxes of 6 ampoules of 2 cc.*

In moderate to severe pre-eclampsia, Veriloid Intramuscular Solution usually produces a prompt reduction of arterial tension to normal limits and quickly relieves associated symptoms. In most patients blood pressure can be maintained at normotensive levels until delivery occurs.

In a recent series† of 56 patients with mild to severe pre-eclampsia, excellent results were obtained in 47 patients, good results in 4, and fair results in 5. In all patients, the blood pressure was depressed until delivery occurred. In 5 cases of postpartum pre-eclampsia, the results were especially gratifying since only a single injection was required for each patient.

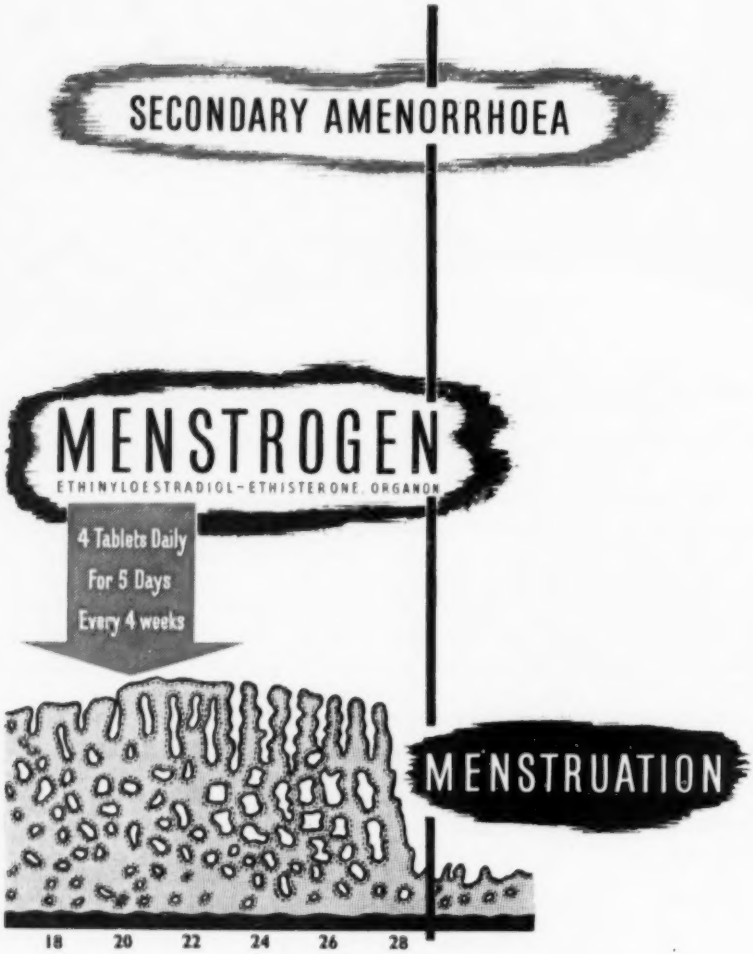
† *Submitted for publication.*

* Trade Mark of

**RIKER LABORATORIES LTD., 29 KIRKEWHITE STREET, NOTTINGHAM**

Detailed information gladly sent on request

***AN ORIGINAL PRODUCT OF RIKER RESEARCH***

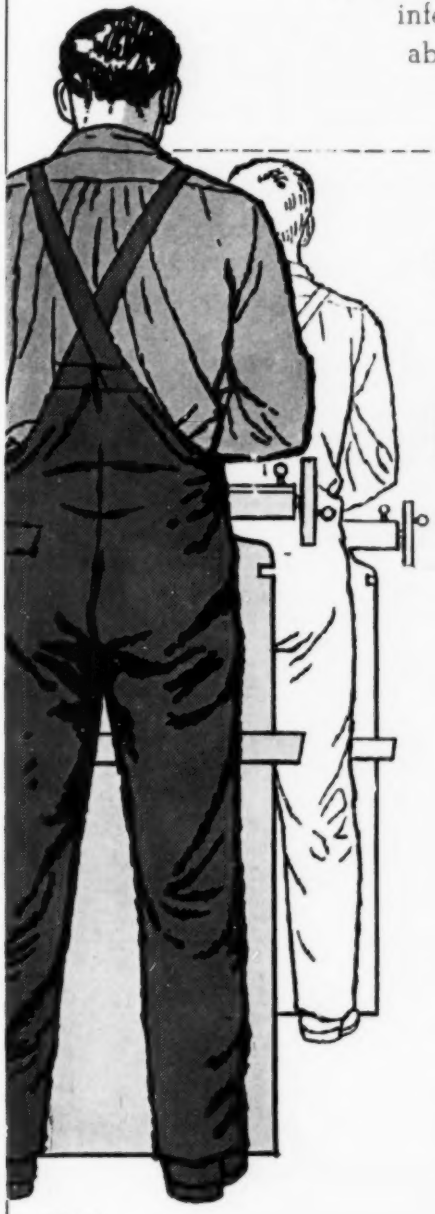



*Packs: 20, 60.*

**ORGANON**
**LABORATORIES LTD.**
BRETTENHAM HOUSE,
LANCASTER PLACE,
LONDON, W.C.2

*Telephone: TEMple Bar 6785 6 7, 0251 2*

**FOR THE PATIENT** with chronic urinary infection who needs to remain up and about 'Mandelamine' and 'Pyridium' play complementary roles.



MUAP104

**'MANDELAMINE'** has an anti-bacterial potency equivalent to that of streptomycin and the sulphonamides without risk of drug-resistance.

**'PYRIDIUM'** gives quick relief from distressing symptoms, by analgesia of the urogenital mucosa, without the depressant effects of narcotics or general sedatives.

Used in combination 'Mandelamine' and 'Pyridium' give both effective antisepsis and gratifying symptomatic relief, with simple oral dosage and no arduous regimen.

***Each 'Mandelamine' tablet contains: 0.25g. (gr. 3¾) methenamine mandelate. Each 'Pyridium' tablet contains 0.1g. (gr. 1½) phenyl-azo-α-α-diamino-pyridine hydrochloride.***

*'Mandelamine' and 'Pyridium' are the registered trade marks of Nepera Chemical Co. Inc.*

**MENLEY & JAMES, LIMITED**
**Coldharbour Lane, London, S.E.5**

# *Bloodless revolution*

The introduction of 'Dextraven' has made available for the first time a dextran solution with controlled optimal molecular content which has been referred to as "narrow fraction dextran". It produces rapid elevation and prolonged maintenance of blood volume and normally ensures that over 50% of the dextran administered remains in the circulation after 24 hours—a longer period than has been possible with any other previous blood volume restorer. 'Dextraven' is the preparation of choice for the restoration of blood volume. The British Encyclopædia of Medical Practice (Medical Progress, 1952) states —" There is little doubt that the narrow fraction dextran will revolutionise supportive therapy and may be regarded as one of the major advances of the year ".—Truly a bloodless revolution.

# Dextraven TRADE MARK

*Developed by* **research** *at*

**Benger Laboratories**

**BENGER LABORATORIES LIMITED · HOLMES CHAPEL · CHESHIRE · ENGLAND**

# Dienoestrol Cream

(Ortho)

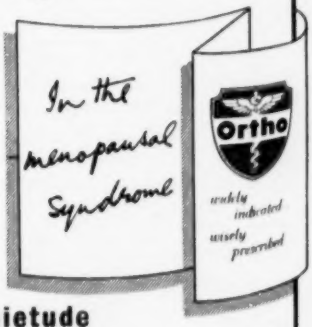
VAGINAL OESTROGEN THERAPY

**in atrophic and senile vaginitis and postmenopausal pruritis vulvae**

By maximum concentration at the point of need and rapid absorption into the vaginal epithelium, Dienoestrol Cream (Ortho) quickly controls symptoms in senile vaginitis, postmenopausal pruritis and atrophic vaginitis. Diminished risk of oestrogen-induced bleeding and freedom from untoward reactions have been noteworthy in patients using Dienoestrol Cream (Ortho) over long periods.

DOSAGE: One applicatorful per day for one or two weeks, reduced to one applicatorful every 48 hours for a similar period.

On original prescriptions specify "Dienoestrol Cream (Ortho) with applicator".




LITERATURE ON REQUEST

# hexital

**for menopausal disquietude**

By combating both nervous and endocrine symptoms simultaneously, Hexital provides simplified, efficient management of the menopausal patient. Combining the highly active and exceptionally well-tolerated oestrogen hexoestrol 3 mg. with the mild sedative phenobarbital 20 mg. (1/3 gr.), Hexital therapy is convenient and economical.

DOSAGE: One tablet daily on retiring for the average case, increased to 2 or 3 tablets daily in severe cases. Hexital is supplied in bottles of 100 and 500 scored tablets.

**Ortho** *Pharmaceutical Limited*

HIGH WYCOMBE · BUCKINGHAMSHIRE · ENGLAND. *Makers of Gynaecic Pharmaceuticals*

# TERRA FIRMA

The treatment of hæmorrhoids rests on solid therapeutic grounds when it achieves relief without resort to narcotic or anæsthetic agents; these may mask the symptoms of more serious pathological conditions. Anusol' Suppositories give relief that is completely safe through decongestion, lubrication and protection. They remove inflammatory pressure on the nerve endings, soothe irritation and guard against the complications of bleeding and infection.

Another notable feature of Anusol Suppositories is the economy of the treatment. It is an impressive fact that Anusol Suppositories, dispensed from bulk by a chemist, are less expensive than their National Formulary equivalent. Anusol Suppositories may be confidently prescribed in the knowledge that they represent a most reliable and economical treatment for all uncomplicated hæmorrhoidal conditions.

*Anusol Haemorrhoidal Suppositories are obtainable from all chemists in boxes of 12; also available in packages of 100 for dispensing only, free of purchase tax when prescribed either privately or on the N.H.S. The tax free package of 100 Anusol Suppositories is supplied to the chemist at 15s. 3d. net. Anusol Ointment is supplied to chemists in tubes containing approximately 1 oz.*

**Anusol**
★ TRADE MARK REGD.

Bism. Subgall. 2·12%, Bism. Oxid. 0·87%, Resorcin 0·87%, Bism. Oxyiodogall. 0·03%, Acid. Boric 17·85%, Zinc. Oxid. 10·60%, Bals. Peruv. 1·77%

**NO WARNER PREPARATION HAS EVER BEEN ADVERTISED TO THE PUBLIC**

*William R.* **WARNER** *and Co. Ltd. Power Road, London W.4.*

# 'B.W.&CO.' Obstetric Products

**PETHIDINE HYDROCHLORIDE 'B. W. & CO.'**

The obstetric analgesic of choice. Pethidine hydrochloride is rapidly effective, is free from toxic effects on mother and child and does not interfere with the normal course of labour.

**'WELLCOME'** BRAND Injection of **HEXŒSTROL DIPROPIONATE**

An esterified form of hexœstrol with important advantages for inhibiting or suppressing lactation. A single injection is sufficient in the majority of cases.

**'STILBOFAX'** BRAND **STILBŒSTROL OINTMENT**

For use where local œstrogen therapy is indicated. 'Stilbofax' is especially valuable as an ante-natal and puerperal lubricant for the nipples.

**ERGOMETRINE MALEATE, 'B. W. & CO.'**

The drug of choice for all obstetric conditions in which the characteristic action of ergot is desired. Ergometrine Maleate is free from toxic effects on the vascular and autonomic systems.

**'INFUNDIN'** BRAND **PITUITARY** (Posterior Lobe) **EXTRACT**

A stable extract of posterior pituitary recommended for use in certain obstetric emergencies when it is desired to overcome uterine inertia.

**'LUBAFAX'** BRAND **STERILE SURGICAL LUBRICANT**

An improved surgical lubricant with a wide range of usefulness in obstetric practice. Smooth, colourless and non-irritant, 'Lubafax' may be readily applied to instruments, hands or rubber gloves.

**BURROUGHS WELLCOME & CO.** (The Wellcome Foundation Ltd.) **LONDON**

# The economics of antenatal care

**To provide enough of all the essential protective factors and at the same time to avoid unnecessary excess is the aim in prescribing for pregnancy. Supplementation is needed to maintain full health and to guard against such complications as, for example, toxaemia, premature births, hypochromic anaemia, inability to breast feed and dental caries.**

**By combining in one preparation all the factors needed to ensure adequacy, not only is economy effected but the patient is not burdened by excessive medication.**

*FORMULA: The daily dose provides, at time of manufacture:*

| | | | |
|---|---|---|---|
| *liq.vitamin A conc., B.P.(40mg.)* | 2,000 *i.u.* | *ferr. sulph. exsic., B.P.* .. | 204 *mg* |
| *liq.vitamin D conc., B.P.(30mg.)* | 300 *i.u.* | *calc. phosph., B.P.* .. .. | 480 *mg* |
| *vitamin $B_{12}$, B.P.* .. .. | 0.6 *mg.* | *pot. iod., B.P. not less than* .. | 15 *p.p.m* |
| *vitamin C, B.P.* .. .. | 20 *mg.* | *cupr. sulph., B.P.* .. } *not less than* | |
| *tocoph. acet., B.P.C.(vitamin E)* | 1 *mg.* | *mang. sulph., B.P.C.* .. } 40 *p.p.m.* | |
| *nicotinamide, B.P.* .. .. | 25 *mg.* | | |

***Cost of Prescribing***

*All V.L. specialities are prescribable under the N.H.S. The cost is in no case greater, and in some cases less, than the official preparation. There is no official equivalent of some V.L. specialities.*

# PREGNAVITE

*a single supplement for safer pregnancy.*

*Clinical sample and medical literature may be obtained on application to :—*

VITAMINS LIMITED (Dept. C.43), UPPER MALL, LONDON, W.6

# A new pleasantly flavoured elixir for the menopausal patient

## 'MEPILIN' HITHERTO ISSUED AS TABLETS IS NOW ALSO AVAILABLE AS AN ELIXIR

The association of methyltestosterone and ethinylœstradiol in Mepilin produces a more complete response in the treatment of menopausal disorders than can be obtained by the use of œstrogens alone.

The presence of methyltestosterone enables a reduction in œstrogen dosage to be made; thus undesirable side effects such as breast turgidity and pelvic congestion are avoided and the risk of withdrawal bleeding is reduced. An increased feeling of confidence and well-being is produced which is both mental and physical.

## 'MEPILIN' TABLETS & ELIXIR

*Each teaspoonful (4 ml.) of Mepilin Elixir and each Mepilin Tablet contains ethinylœstradiol 0.01 mg. and methyltestosterone 3 mg.*

| | |
|---|---|
| 'MEPILIN' TABLETS<br>Bottle of 25 at 4/4 and 100 at 14/6<br>'MEPILIN' ELIXIR<br>Bottle of 4 fl. oz. at 6/- and 20 fl. oz. at 23/-<br>*Basic N.H.S. price* | DOSAGE: Menopause and geriatric conditions: average cases—3 tablets or 3 teaspoonfuls daily. Premenstrual tension and dysmenorrhœa—2 tablets or 2 teaspoonfuls daily from 10th to 22nd day of the menstrual cycle. |

*Literature and specimen packings are available on request*

THE BRITISH DRUG HOUSES LTD. (Medical Department) LONDON N.1

MEP/E/4

# TAMPOVAGAN

Tampovagan pessaries are designed for one of the most difficult problems facing the Medical Profession—the treatment of vaginal discharge—Leucorrhoea.

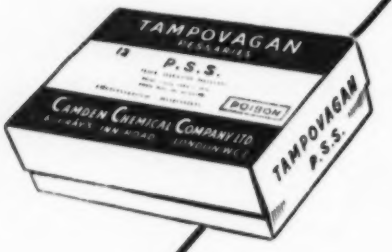
Camden Research has produced 10 varieties of easily soluble pessaries—with recent additions made at the special request of the Medical Profession—making Tampovagan therapy a comprehensive, up-to-date, and highly efficient treatment for all types of Leucorrhoea.

*Packings*: Containers of 12, 50 and 100.

*Prescriptions*: May be prescribed on form E.C.10.

(*a*) Tampovagan with lactic acid 5%
(*b*) Tampovagan with ichthyol 5%
(*c*) Tampovagan with ichthyol 10%
(*d*) Tampovagan with choleval 1%
(*e*) Tampovagan with penicillin 5,000 i.u.
(*f*) Tampovagan with penicillin 100,000 i.u.
(*g*) Tampovagan with P.S.S. (penicillin, sulphanilamide and sulphathiazole)
(*h*) Tampovagan with stilboestrol and sulphathiazole[1]
(*i*) Tampovagan with 0.5 mg. stilboestrol
(*j*) Tampovagan with 0.5 mg. stilboestrol and 5% lactic acid

[1] O'Sullivan, *The Practitioner*, No. 986, August 1950




## for Leucorrhoea

Literature and samples available to the Medical Profession

**CAMDEN CHEMICAL COMPANY LTD.**
**61, GRAY'S INN ROAD · · · LONDON W.C.1**

*Sole Agents in South Africa*—Westdene Products (Pty.) Ltd., 22-24 Essanby House, Jeppe Street, Johannesburg

# *The outlook need not be clouded...*

... by the shadowy fear of the menopause and its associated vasomotor and psychic disturbances.

Euvalerol M, the ideal sedative in menopausal conditions, ensures that the difficult years may be contemplated with equanimity and passed through with ease.

Symptoms of apprehension, flushing, irritability and depression that darken the outlook of the woman at the menopause are alleviated, and the emotional balance restored, by the administration of Euvalerol M.

Euvalerol M contains an odourless preparation of valerian with ¼ grain (16 mg.) phenobarbitone and 0·1 mg. stilbœstrol in each fluid drachm.

# EUVALEROL M

In bottles of 4 and 8 fluid ounces.

Literature on application.

ALLEN & HANBURYS LTD · LONDON · E·2

TELEPHONE BISHOPSGATE 8201 (20 LINES). TELEGRAMS "GREENBURYS, BETH, LONDON"

# NOTICES

THE JOURNAL OF OBSTETRICS AND GYNAECOLOGY OF THE BRITISH EMPIRE was established in 1901 by a group of British Obstetricians and Gynaecologists, and the profits earned have been devoted to the maintenance and improvement of the Journal. In January 1951 the Journal was transferred by purchase to the Royal College of Obstetricians and Gynaecologists.

The publishers and printers are Messrs. John Sherratt and Son, Park Road, Altrincham. The annual subscription is £3 5*s*. for Great Britain and Northern Ireland and £3 15*s*. for the Dominions, Colonies, and Foreign Countries. It is payable to the Royal College of Obstetricians and Gynaecologists at 58 Queen Anne Street, London, W.1. Overseas subscribers should remit by draft payable in London or through the usual agents.

Books for review should be sent to the Editor. The right of publication of all articles is reserved.

## Directions to Contributors

Original articles for publication are invited and should be sent to the Editor, Professor James Young, "Ashfield," Balcombe Road, Haywards Heath, Sussex. They are accepted on the understanding that they are contributed to this Journal only. Authors are advised to keep a copy of all manuscripts. Proofs will be submitted to authors resident in the United Kingdom, but to avoid delay or loss the proofs of authors resident abroad will be corrected by the editorial staff, unless the authors wish to delegate the work to a representative in this country. To lessen editorial work it is desirable that authors conform to the following conventions:

### PRESENTATION OF MANUSCRIPT

Double spaced typescript (not carbon copies) should be submitted. Italics in the text should be reserved for words in a foreign language and as little as possible used to indicate emphasis.

Proper scientific names giving both genus and species should be italicized, with an initial capital and contraction for the genus only after a full spelling at the first mention, thus:

*Clostridium welchii* followed by *Cl. welchii; Bacterium coli—Bact. coli; Bacillus tuberculosis — B. tuberculosis; Corynebacterium diphtheriae—C. diphtheriae.*

Each sentence should have its proper components thus:

"*Progress*: The patient continued to improve."

NOT

"*Progress*: Went downhill."

The author's name, his decorations, degrees and relevant diplomas should appear at the head of the paper together with his appointment at the time of preparation of the text.

### TABLES AND ILLUSTRATIONS

Tables should be numbered in Roman numerals (Table I, Table II, etc.) and set out on sheets separate from the text, with indications as to where the author desires them to be placed. Illustrations, too, should be kept separate from the text and numbered in Arabic numerals, Fig. 1, Fig. 2, etc. Each figure should have a reference in the text and a descriptive legend to be printed underneath. This legend should be typed on an attached sheet and not written on the back of the illustration. The lines in charts should not be in colours but in black, and when graph paper is used the ruling should be grey or faint blue and *not* brown, red or green. The magnification of microscopical illustrations should be stated (e.g., × 250). X-ray films should not be submitted unless the author is not in a situation to have these printed, when the Journal will undertake to have this done. If the films promise poor reproduction the author is advised to send line tracings of the appearances instead. Authors may be required, at the Editor's discretion, to contribute to the cost of reproducing half-tone or coloured plates.

### ABBREVIATIONS

These should be avoided as far as possible. Thus "per cent" should be used instead of the symbol "%" and such forms as T.B., R.B.C., B.P., P.E.T., A.P.H. eschewed.

Dates should be given as 10th May, 1946, and *not* 10. V. 46. Numbers should be in the form of numerals and not words except when beginning a sentence, thus "Fifteen patients out of a total of 60 exhibited," etc. The official rather than the proprietary names of drugs must be used. The Journal convention is gr. for grains; g. for grammes; Kg.; ml. (*not* c.c. or c.cm.); mg.; pounds (*not* lb.); ounces (*not* oz.), etc., and wherever suitable the metric equivalent of an English measure should be given, for example, when recording pelvic measurements, size and weight of babies, tumours, etc.

When comparable figures are given, either the English or the metric mode must be followed, thus: the excretion of urine/24 hours should be shown in ml. (and not ounces) when the urinary or blood-urea is given in g./100 ml.

### REFERENCES

In the text the author's name should be given, with the date of publication and the list of authors quoted put at the end of the text in alphabetical order as in the Harvard Scheme: Author's name, initials, year of publication (in brackets), name of journal (*italics* abbreviated), volume number (underlined) and page number. In the case of books the order is: Author's name, initials, year of publication, full title (*italics*), edition, publisher and place of publication, page, thus:

Brown, H. E., and Jones, B. K. (1943): *J. Obstet. Gynaec. Brit. Emp.*, **2**, 128.

Sampson, P. (1940): *Obstetrics for Midwives*. 2nd edition. Fraser, London. p. 9.

### REPRINTS

Twenty-five reprints for each author are supplied free of charge. An author may purchase additional reprints if he notifies the publishers on the form attached to the proof of his paper.

Contributors from overseas should state the required number on their manuscript.

# AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY

*Representing*
THE AMERICAN GYNECOLOGICAL SOCIETY,
THE AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS,
AND TWENTY-SIX OTHER SOCIETIES

*Editors* — *Advisory Editor*
H. C. TAYLOR, JR. W. J. DIECKMANN G. W. KOSMAK

Because it is the American Journal devoted exclusively to Obstetrics and Gynaecology, this Journal, alone, offers you complete coverage on all the developments constantly being made in these fields in America. Abstracts of the important literature from all parts of the world are published. Most of the outstanding medical schools in the United States are represented on the editorial board, which consists of forty-two of the leading teachers and practising specialists in America.
The two volumes published annually contain approximately 2,200 pages and have about 500 illustrations. They constitute a complete record of progress and achievement for the period.

**Published Monthly.** **Annual subscription £6 5s. 0d. per annum, post free; single copies, 15s. 0d.**

THE C. V. MOSBY COMPANY, PUBLISHERS, ST. LOUIS
*AGENT FOR GREAT BRITAIN*
HENRY KIMPTON ∴ MEDICAL PUBLISHER
**25 Bloomsbury Way - London, W.C.1**

---

## ATLAS OF MAHFOUZ'S OBSTETRIC AND GYNAECOLOGICAL MUSEUM

by

NAGUIB PACHA MAHFOUZ

M.Ch., F.R.C.O.G. (Hon.), F.R.C.P. Lond., F.R.C.S. Eng. (Hon.)

Three volumes, containing over 200 plates in full colour and over 500 in black and white. Each plate is described in English, Arabic, French, German, Italian, Russian, Spanish. Three volumes. Strongly bound. Over 1200 pages

**Price per set, £9 9s. 0d. net (Canada and the U.S. of America, $40, post free)**

*The volumes are not sold separately*

A similar collection has—to the reviewer's knowledge—never been presented hitherto. It makes a distinct, original, and valuable contribution to obstetric and gynaecological pathology which should be in every medical library and that of the gynaecological and obstetric specialist."—I. C. RUBIN

*The American Journal of Gynecology and Obstetrics*, April 1951

JOHN SHERRATT AND SON, PUBLISHERS, ALTRINCHAM, ENGLAND

*Spencer provides "Hammock-like" support for the growing uterus, comfort and protection for back and breasts*

# *" Did nature intend the pregnant woman to wear a support—?"*

No—just as nature did not intend her to require additional nutrients, hormones, stimulants, or sedatives! But under to-day's stresses and strains, nature's intentions often fall short, so *proper* supports — like medicines — have their place in modern therapy.

Spencer supports will provide greater therapeutic benefits for your *average* antepartum-postpartum patients — as well as for those with backache or other symptoms — because:

Each Spencer Support is *individually designed, cut and made* for each patient to meet individual medical indications.

We invite your trial of Spencer Supports for men, women and children, too.

*For further information write to—*

**SPENCER (BANBURY) LTD.**

*Consulting Manufacturers of*

**SURGICAL AND ORTHOPAEDIC SUPPORTS**

**Spencer House : Banbury : Oxfordshire**

**Tel : Banbury 2265**

**BRANCH OFFICES AND FITTING CENTRES:**

| | |
|---|---|
| **LONDON :** 2, South Audley Street, W.1 | Tel: GROsvenor 4292 |
| **MANCHESTER :** 38a, King Street, 2 | Tel: BLAckfriars 9075 |
| **LIVERPOOL :** 79, Church Street, 1 | Tel: Royal 4021 |
| **LEEDS :** Victoria Buildings, Park Cross Street, 1 (Opposite Town Hall steps) | Tel: Leeds 3-3082 |
| **BRISTOL :** 44a, Queens Road, 8 | Tel: Bristol 24801 |
| **GLASGOW :** 86, St. Vincent Street, C.2 | Tel: Central 3232 |
| **EDINBURGH :** 30a, George Street, 2 | Tel: Caledonian 6162 |

APPLIANCES SUPPLIED UNDER THE NATIONAL HEALTH SERVICE

*Trained Spencer Retailer-Fitters resident throughout the Kingdom; name and address of nearest Fitter supplied on request*

*Copyright*

J.O.G. 12/53

**EXCERPTA MEDICA**

The International Medical Abstract Service published in English and covering the whole field of Clinical and Experimental Medicine.

**OBSTETRICS AND GYNAECOLOGY**

SECTION X

CONTENTS

All articles appearing in journals devoted to obstetrics, gynaecology and endocrinology (the latter where applicable) are abstracted. In addition to abstracts of articles on the main subjects, abstracts on nursing and infant care, psychosomatic medicine, and on radiology and tuberculosis are included.

*American Journal of Obstetrics and Gynecology.*
*" . . . The Excerpta Medica appear in faultless English . . . "*

*Professor J. P. Greenhill.*
*" . . . May I say that your Section X of Excerpta Medica is excellent . . . and I therefore cannot offer any suggestions for its improvement. I believe you and your co-editors are doing a magnificent job . . . "*

The subscription rate is £3 15s. per yearly volume of 600 pages, including an index classified both by author and subject. Write for a prospectus or specimen copy.

*Sole Distributors for Great Britain and the British Dominions:*
E. & S. LIVINGSTONE, LTD., 16–17, TEVIOT PLACE, EDINBURGH, 1.

Send your copies of the

Journal of Obstetrics & Gynaecology of the British Empire

for **BINDING** to

JOHN SHERRATT & SON
PARK ROAD, ALTRINCHAM

# *Not whether but how*

FERROUS SULPHATE *is now recognised as the most efficient form of iron treatment for hypochromic anæmias.* The question is therefore not "*whether*" but "*how*" it should be administered.

The preparation should not be too bulky, nor cause gastro-intestinal upset, yet it must disintegrate quickly and produce maximum hæmatopoietic response.

In 'PLASTULES' ferrous sulphate is presented in its most attractive form—in a semi-solid base in a capsule which rapidly dissolves in the stomach, thus ensuring maximum absorption. 'PLASTULES' induce a rapid response without gastric upset.

'PLASTULES' *are available in four varieties: Plain:* with *Liver Extract:* with *Folic Acid:* and with *Hog's Stomach.*

## 'PLASTULES' *Hæmatinic Compound*

*Trade Mark*

JOHN WYETH & BROTHER LTD., CLIFTON HOUSE, EUSTON ROAD, N.W.1

Wyeth

## ERRA

Harrison, R. G., and Malpas
*Gynaec. Brit. Emp.*, **60**, 6

"The Volume of Human
*column 2, (6), line 18.*

$$\text{Surface area} = 2\pi ab \left( \frac{s}{} \right.$$

where $e$ = the eccentricit

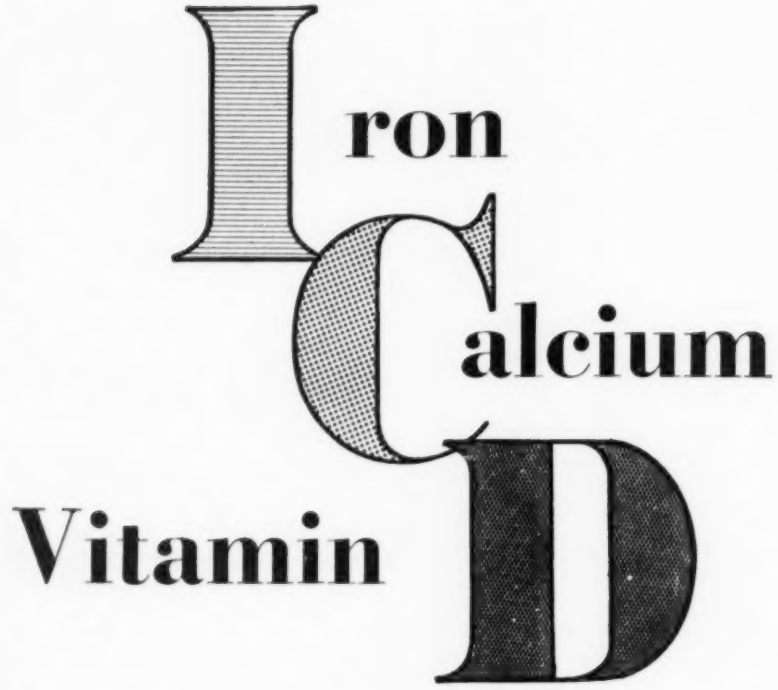
## RATUM

Malpas, P. (1953): *J. Obstet*
**60**, 632–639.

man Amniotic Fluid," *p. 634,*
*18.*

$$b\left(\frac{\sin^{-1} e}{e} + \sqrt{1-e^2}\right)$$

tricity, which $= \sqrt{1 - \frac{b^2}{a^2}}$




Immediately pregnancy is confirmed, the mother should realise that an adequate daily intake of iron, calcium and vitamin D is of very special importance during the months ahead. Caldeferrum Tablets are specifically prepared to meet this need. Taken as a routine throughout pregnancy and lactation, four Caldeferrum Tablets daily supply the mother's estimated requirement of iron, a large part of her calcium needs, and ample vitamin D for proper assimilation of the calcium. The tablets are small, sugar-coated and easy to take.

**CALDEFERRUM**
TABLETS

*One tablet four times daily throughout pregnancy and lactation. Containers of 100 and 1,000.*

GLAXO LABORATORIES LIMITED, GREENFORD, MIDDLESEX BYRon 3434

The Journal of
Obstetrics and Gynaecology of the British Empire

Vol. 60, No. 6 NEW SERIES DECEMBER 1953

# TOXOPLASMOSIS AND PREGNANCY

BY

SVANTE C:SON HOLMDAHL, M.D.

*Assistant Obstetrician and Gynaecologist*

*From the Medical Department of the Göteborg Children's Hospital and the Gynaecological Departments, the H Institute of Pathological Anatomy and the Virus Laboratory of the Sahlgrenska Hospital, Göteborg, Sweden*

## INTRODUCTION

A LARGE number of cases of infantile toxoplasmosis, the disease defined by Wolf and his colleagues (Wolf, Cowen and Paige, 1939; Wolf and Cowen, 1939; Paige, Cowen and Wolf, 1942; Cowen and Wolf, 1945), have been reported during the last 10 years. Frenkel and Friedlander (1951), Sabin (1942, 1948), Piekarski (1950), Thalhammer (1951) and others have collected these cases and assembled the results of microbiological research on animals.

The frequency of antenatal inception of toxoplasmosis in human beings has not yet been given thorough study. The present investigation aims to throw light on the question of how often toxoplasmosis is responsible for abortion, intra-uterine death of the foetus, neonatal disease and death, and infantile disease and malformation. The diagnostic value of serological tests for toxoplasmosis in antenatal care and obstetrics will also be discussed and likewise the manner of antenatal inception of toxoplasmosis. The possibilities of preventing intra-uterine toxoplasmosis and whether or not antenatally diagnosed toxoplasmosis justifies termination of pregnancy are two other problems which will be scrutinized.

## SURVEY OF LITERATURE

It has been established by experiments on animals that the microbes are spread by the blood to the different parts of the body during the first two weeks after infection. While this goes on, a rapidly increasing titre of antibodies can be demonstrated. It appears that the distribution of microbes by way of the maternal blood begins to cease when antibodies appear in the circulation and, when they reach a high level, the parasites are only found sporadically in the tissues and in an inactive form as intracellular aggregations (Cowen and Wolf, 1950, 1951).

Antibodies to Toxoplasma have been found in a large number of presumably healthy persons, the frequency varying from a few to 50 per cent of the subjects examined (Callahan *et al.*, 1946; Holmdahl, 1949; Kunert and Jüptner, 1952; Macdonald, 1949; Piekarski, 1950; Sabin, 1942). They can be demonstrated with several different methods. Only three of them will now be mentioned. In Sabin's rabbit test and the egg test worked out independently by Alm (1948) and Macdonald (1950) the serum's capacity to inhibit the activity of living Toxoplasma is estimated. The egg test has proved to be the better of these two tests. In the dye test of Sabin and Feldman (1948), the method most used nowadays, the antibody strength is determined by a microbiological staining method. The results of the egg and dye tests are equal as regards quality, but the dye test seems to give more accurate quantitative results (v. Zeipel and Linder, 1951).

After infection with toxoplasmosis, the dye

test titre rises to a high level (Bengtsson, 1950; Gard *et al.*, 1949, 1952; Jelke, 1950; v. Zeipel and Linder, 1951). The high titres seem to persist for at least 6 months, and then sink slowly over a period of several years. It has been possible to demonstrate antibodies as late as 10 years after infection.

In the case of pregnancy there is obviously a risk of infection of the foetus during the acute phase when the parasites are present in the maternal blood. This has been borne out by several experimental studies on animals (Cowen and Wolf, 1950, 1951; Eichenwald, 1948; Jacobs and Jones, 1950). On the other hand, it is not certain whether the microbes can infect the foetus after the parasites have left the blood. Some authors maintain that a high antibody titre means a large risk of infection of the foetus. Others maintain that it protects the foetus from latent toxoplasmosis (Holmdahl, 1951, 1952; Macdonald, 1950), pointing out that the number of women with a high antibody titre is large in comparison with the few cases of infantile toxoplasmosis observed.

The clinical picture of infantile toxoplasmosis includes internal hydrocephalus, intracerebral calcification, chorioretinopathy and psychomotor disorders. In acute and sub-acute cases there are also changes in the cerebrospinal fluid with monocytic pleocytosis and an elevated protein content. Occasionally, however, the picture is dominated by intestinal symptoms with enlargement of the liver and spleen and jaundice. These signs are often present at birth, but in many cases do not appear until weeks or months have passed. According to Sabin and Feldman (1949), intracerebral calcification is always present.

It is still uncertain whether toxoplasmosis can cause abortion. There are a few cases reported in which a woman had a miscarriage directly before or after giving birth to a baby with toxoplasmosis. However, it has not been possible to prove that Toxoplasma caused the miscarriages. A number of cases of intra-uterine foetal death have been ascribed to toxoplasmosis, the assumption being based on evidence of the infection in the maternal serum. In my opinion, none of these cases is sufficiently authenticated. Cowen and Wolf (1950, 1951) showed in animal experiments, however, that Toxoplasma can lead to specific inflammatory lesions in the foetus and intra-uterine death. Analysis of the responsibility of toxoplasmosis for human intra-uterine mortality must be done by statistical procedures, for autolysis leads to the obliteration of any inflammatory changes present.

Ever since cases of antenatally acquired toxoplasmosis were first demonstrated, it has been assumed that the microbes are transferred to the foetus via the placenta, but not until recently has it been possible to establish this fact. Cowen and Wolf (1950, 1951) showed by extensive experimental studies on pregnant mice that specific inflammatory lesions occur in the placenta during the second week of infection. However, they could not find a single instance of renewed dissemination to the placenta by the blood stream after the infection had been checked by antibodies.

On the other hand, every attempt to transfer Toxoplasma by way of the placenta to the foetus in primates has failed. Even when pregnant monkeys were inoculated with Toxoplasma 2 or 3 weeks before delivery, the infection was not spread to the foetus. The negative results may be due to the fact that only small series of experimental animals could be used (Cowen and Wolf, 1950).

Despite the fact that hundreds of cases of congenital toxoplasmosis in humans are reported, only 2 are described in which the mother showed signs of acute infection during the latter part of pregnancy, the 7th and 8th month, respectively (Adams, 1948; Farquhar and Turner, 1949). These 2 women had multilocular tender and inflamed lymph nodes and a finely mottled eruption. The signs and symptoms of toxoplasmosis in the adult do not seem to differ from those of a mild infection (Plaut, 1946; Tomlinson, 1945). The majority of persons with serological evidence of recent toxoplasmosis can never relate anything of note.

## Present Study

### *Material*

The present study covers the 23,260 babies born at the two maternity hospitals in the city of Göteborg during the years 1948 to and includ-

ing 1951. They represent about 95 per cent of the children born in Göteborg during this period. Of these, 633 were stillborn or died within a week after birth. All the foetuses classed as stillborn were at least 35 cm. long. All these 633 children were autopsied. The central nervous system was examined with the naked eye and a few sections studied microscopically, except in cases of great maceration, anencephaly and cranioclasis. When inflammatory changes were present, more extensive microscopical study was made.

All the living children were examined by paediatricians on at least two occasions during the first week of life. About 21,000 of them were followed up regularly during the first year by paediatricians at the city child welfare clinics. On any signs of cerebral lesion the children were sent to the medical department of the Göteborg Children's Hospital.

The study also includes a serological study of a large number of women. One series, which I described in an earlier study (Holmdahl, 1949), includes the following cases, collected successively as they came to the maternity hospitals: 108 women with children born dead or dying soon after birth, 113 women giving premature birth, 101 women with an inexplicable abortion in the 2nd to 6th months, and 32 women giving birth to children with major developmental defects. The serological examination of these women was undertaken with the egg test. The children were examined on the lines just described. Whenever the mother had an antibody titre of 100 or more, however, the central nervous system of the child was given a more thorough histopathological examination if it was stillborn or died shortly after birth. If it was alive, its skull was roentgenographed and its eyes examined with the ophthalmoscope.

For control purposes, 233 women with a normal delivery and normal children were examined with the egg test as well as 94 presumably healthy non-pregnant women. The latter were included to see whether pregnancy was associated with non-specific antibody formation.

The second series consists of 415 women chosen at random from the ones coming to the out-patient department for antenatal care. These women were examined with the dye test and 270 of them with repeated tests until their child was born. Furthermore, 93 women with abortions in the 2nd to 6th months were examined with the dye test, one test at the time of the miscarriage and another 2 to 6 weeks later.

In addition, 59 aborted ova and 158 placentas were examined histopathologically and any inflammatory changes discovered checked with the antibodies in the maternal serum.

*Serological Methods*

The two serological tests for Toxoplasma-neutralizing antibody used in this study are described by von Zeipel and Linder (1951) in a publication from our virological department. In the egg test, the strength of titre is given as the ratio between the average number of Toxoplasma colonies in the negative serum controls and in the serum tested. In the dye test, the titre is given as the highest dilution of serum with which at least 50 per cent of the microbes are injured by the antibodies.

*Results of Investigation*

Two cases of infantile toxoplasmosis were discovered in the 23,260 children born at the maternity hospitals in Göteborg during the years 1948 to and including 1951. They will now be briefly described.

CASE 1. A primigravida aged 17 had an uneventful pregnancy and a child weighing 3,400 g. was normally delivered at term. A week later it was reported to be well. The mother noticed shortly after birth, however, that one eye was smaller than the other. Breast-feeding was satisfactory and the child gained 500 g. in 7 weeks. At 8 weeks it was noted that the circumference of the skull had increased from 38 cm. at birth to 44.5 cm. Other abnormalities noted were bilateral microphthalmus, bilateral healed chorioretinitis and intracranial lunate calcifications. Ventriculograms revealed severe internal hydrocephalus. The cerebrospinal fluid was clear and contained a large amount of protein but a normal amount of cells and no Toxoplasma. The antibody titres of the mother and child can be seen from Fig. 1.

CASE 2. A multipara aged 32 had had 2 normal deliveries 12 and 6 years previously and both children were living and well. She suffered from sore throat on several occasions during pregnancy. A month before delivery the children brought home some baby birds which died in the house. The patient got another sore throat at this juncture and a few weeks later, in the

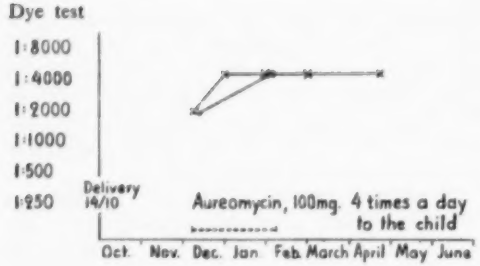



FIG. 1

Serological data from Case 1. o———o titre curve for mother, x——x titre curve for child.

8th month of pregnancy, she gave birth. The baby was extremely immature and cyanotic and had an abnormally large spleen and liver. It died 3 hours after birth. Autopsy revealed pulmonary atelectasis with exudate in the pleurae and pericardium. The spleen and liver were enlarged and congested. The meninges were hyperaemic and the subdural space contained a large amount of clear golden brown fluid. The cerebral parenchyma was congested and disintegrating, and presented numerous soft and granulated foci of all sizes up to that of a hazel nut. The microscope showed meningo-encephalitis with extensive necrosis and calcification, areas infiltrated by lymphocytes and plasma cells, and in one section intracellular accumulations of parasites corresponding in size and shape to Toxoplasma (Fig. 2). The dye test titre in the maternal serum was 1:4000 three days after delivery and 1:2000 four months later. The serum of the child was not examined.

Table I shows the results of the egg test in the 233 women with a normal pregnancy and delivery. The test was made at the time of delivery. It also gives the data from 94 women who said that they had never been pregnant. Table II contains the results of the dye test in 415 women who came to the hospital for antenatal care and in 270 of these women given two or more tests up to the time of their delivery. The latter women are grouped according to the highest titre found in any of the tests.

Ten of the last mentioned women had a titre of 1:250 or more in one of the tests. Table III gives data from 8 of these cases. The other 2 are not included because the titre, never higher than

TABLE I

*Toxoplasma-Neutralizing Antibodies in Healthy Women, Women Aborting in the Second to the Sixth Months and Cases of Obstetrical Abnormality (Egg Test)*

| | No. of cases | < 5 per cent | > 5 Total per cent | > 5 > 100 per cent |
|---|---|---|---|---|
| Women with normal pregnancy and delivery ... ... | 233 | 33.9 | 60.1 | 9.4 |
| Healthy non-pregnant nulliparae ... ... ... ... | 94 | 42.6 | 57.4 | 4.3 |
| Abortions not accompanied by fever ... ... ... | 102 | 43.1 | 56.9 | 2.0 |
| Stillbirth ... ... ... ... ... ... ... ... | 53 | 41.5 | 58.5 | 5.7 |
| Child died shortly after birth ... ... ... ... | 55 | 40.0 | 60.0 | 9.1 |
| Premature birth ... ... ... ... ... ... ... | 113 | 42.5 | 57.5 | 6.2 |
| Major developmental defect in child ... ... ... | 32 | 43.8 | 56.2 | 3.1 |

TABLE II

*Toxoplasma-Neutralizing Antibodies in Healthy Pregnant Women and Women Aborting in the Second to Sixth Months (Dye Test)*

| | No. of cases | Negative result in 1:110 dilution per cent | Positive result in dilution >1:10 per cent | >1:250 per cent |
|---|---|---|---|---|
| Healthy women on first visit for prenatal care during early pregnancy ... ... ... ... ... ... | 415 | 51.8 | 48.2 | 2.4 |
| Group of these given several tests during pregnancy | 270 | 51.5 | 48.5 | 3.8 |
| Miscarriage with and without fever ... ... ... | 93 | 45.2 | 54.8 | 2.2 |

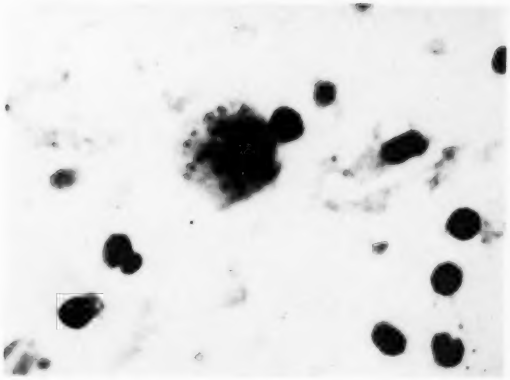


FIG 2
Parasitic cyst in a focal inflammatory and necrotizing lesion in the cerebral white matter.

TABLE III

*Data from 8 Cases in Which Maternal Serum Showed Dye Test Titre of 1:250 or More During Pregnancy*

| Mother | | Child | |
|---|---|---|---|
| Clinical features | Dye test (Roman numerals indicate month of pregnancy) | Clinical features | Dye test |
| 1-gravida aged 24, formerly healthy, had acute bronchitis in fourth month of pregnancy. Pulmonary roentgenograms were normal. | III −1:10<br>V +1:1000<br>VI +1:2000<br>VII +1:4000<br>IX +1:8000<br>5 months after delivery +1:500 | Normal child, normally delivered, weighing 3,090 g. Roentgenograms of skull and ophthalmoscope showed nothing abnormal. Placenta grossly and microscopically normal and cultures gave no Toxoplasma. | Umbilical blood: +1:8000.<br>5 months old: +1:50 |
| 3-gravida aged 37, formerly healthy, had uneventful pregnancy. | IV +1:1000<br>VI +1:2000<br>VII +1:1000<br>X +1:1000<br>5 months after delivery, 1:50 | Normal child, normally delivered, weighing 3,780 g. Roentgenograms of skull and ophthalmoscope showed nothing abnormal. Microscopic study of grossly normal placenta showed foci of leukocytic infiltration. | Umbilical blood: +1:500<br>5 months old: 1:10 |
| 2-gravida aged 20, formerly healthy, had uneventful pregnancy. Delivered at another hospital. | VIII +1:2000<br>X +1:1000<br>5 months after delivery, +1:1000 | Normal child, normally delivered, weighing 3,540 g. Roentgenograms of skull and ophthalmoscope showed nothing abnormal. | 3 months old: +1:500<br>6 months old: +1:10 |
| 1-gravida aged 37, had typhoid fever 6 years earlier. Gave premature birth. Emigrated to the U.S.A. after discharge from hospital. | VII 1:250<br>VIII 1:500 | Premature child developed uneventfully and was discharged healthy. | |
| 4-gravida aged 37, formerly healthy, had uneventful pregnancy. | III +1:500<br>IV +1:250<br>VI +1:250<br>X +1:50<br>3 months after delivery, 1:2000 | Normal child, normally delivered, weighing 4,000 g. | 3 months old: +1:10 |
| 1-gravida aged 21, had gonorrhoea just before conception. Uneventful pregnancy. | III +1:1000<br>IV +1:250<br>V +1:2000<br>VI +1:1000<br>3 months after delivery, +1:2000 | Normal child, normally delivered, weighing 3,750 g. Roentgenograms of skull and ophthalmoscope showed nothing abnormal. | 3 months old: +1:50 |
| 1-gravida aged 19, formerly healthy, had uneventful pregnancy. | III +1:2000<br>IV +1:1000<br>VI +1:1000<br>4 months after delivery, +1,1000 | Normal child, normally delivered, weighing 3,060 g. | 4 months old: +1:10 |
| 1-gravida aged 21, formerly healthy, had uneventful pregnancy. | IV +1:50<br>VI +1:250<br>VII +1:250<br>X +1:500<br>4 months after delivery, +1:50 | Normal child, normally delivered, weighing 3,430 g. Placenta grossly and microscopically normal. | 4 months old: +1:10 |

1:250, decreased successively with every test. All the children of the women in Table III were healthy and exhibited no signs of toxoplasmosis.

The first woman in the table is particularly interesting as she seems to have acquired toxoplasmosis during pregnancy. The first dye test gave negative results, but the following ones gave positive results, the titres rising continuously to 1:8000. The rise began in the 4th month in connection with acute bronchitis. Roentgenograms of the lungs were normal and none of the signs typical of acute toxoplasmosis in the adult was manifested.

Two separate series of women aborting in the 2nd to 6th month were examined, one with the egg test (Table I) and the other with the dye test (Table II). The first group were examined with only one test after the abortion, the second one with at least two tests, one after the abortion and the others 2 to 6 weeks later to see whether the titre rose after the abortion. The first group had a temperature below 38°C. at the time of the abortion, but about half the other women had a temperature over 38°C. Cases in which the abortion could be traced to organic or functional defect in the genital organs were not included in these series.

The titres of the women with babies born dead or dying shortly after birth are seen in Table I. A single egg test was made directly after the delivery. The dead children were examined on the lines previously described. Whenever the mother had a high antibody titre, however, several slides from different parts of the central nervous system were examined histologically. No inflammatory change pointing to toxoplasmosis was found in any case.

The antibody level in the 113 women giving premature birth is also seen in Table I. The children weighed 2,500 g. or less and were examined as previously described. No signs of toxoplasmosis were seen in any case.

Table I also includes the 32 women whose children suffered from major developmental defect. In Table IV these cases are grouped according to the nature of the defect. No clinical or histological signs of toxoplasmosis were seen in any of these children. Two of them had internal hydrocephalus without meningocele. The maternal serum contained Toxoplasma-neutralizing antibodies in both these cases. The following is a brief description of them:

(1) A child born healthy at term began to show rapidly progressing hydrocephalus a few days after birth. It died at one year of age with an enormous head. There were no clinical signs of chorioretinitis or encephalo-meningitis, and no evidence of toxoplasmosis was found on pathological examination. An egg test of the mother's serum at the time of delivery revealed a titre of 50, and a titre of 22 in the child at the age of 6 weeks.

TABLE IV

*Toxoplasma-Neutralizing Antibodies in Women whose Children Suffered from Major Developmental Defect*

| Defect | Number of cases | Egg test | | |
|---|---|---|---|---|
| | | < 5 | > 5 Total | > 100 |
| Organic heart disease | 5 | 1 | 4 | – |
| Myelomeningocele with or without hydrocephalus | 4 | 3 | 4 | – |
| Mongolism | 5 | 1 | 4 | – |
| Acrania | 3 | 2 | 1 | – |
| Ocular aplasia | 1 | 1 | – | – |
| Diaphragmatic aplasia | 4 | 3 | 1 | – |
| Atresia of oesophagus | 1 | 1 | – | – |
| Umbilical hernia | 1 | 1 | – | – |
| Hydronephrosis | 1 | – | 1 | – |
| Fibrosis of pancreas | 1 | – | 1 | – |
| Deformity of hands and feet | 4 | 1 | 3 | – |
| Internal hydrocephalus without meningocele | 2 | – | 2 | 1 |

(2) A hydrocephalic child born at term died a few hours after birth. Autopsy revealed foetal chondrodystrophy, internal hydrocephalus and intracerebral haemorrhage. No signs of inflammation or necrosis in the cerebral meninges or parenchyma were found on gross or microscopical examination, nor any evidence of toxoplasmosis. The maternal serum had an egg test titre of 140 ten days after delivery.

It is seen from Tables I and II that none of the various groups had a significantly increased percentage of women with Toxoplasma-neutralizing antibodies. It may be concluded that the differences between them were due to chance.

Fifty-nine ova from the cases of miscarriage in Table I were examined histologically. Infiltration and necrosis were seen in 35 of them, but the changes showed no correlation to the antibody titre in the maternal serum.

The placentas from 158 of the women in Table I were also examined histologically. No correlation was found between infiltration and necrosis in the placenta and the occurrence of antibodies in the maternal serum. The same was true of calcification in the placenta.

## Discussion and Conclusions

### *Frequency of Antenatal Inception of Toxoplasmosis*

Two cases of infantile toxoplasmosis were found in 23,260 newborn children. While some cases may have escaped notice, it is clear that manifest infantile toxoplasmosis is a rare disease.

It is possible, however, that intra-uterine toxoplasmosis may cause the death of the ovum and that the specific inflammatory changes are concealed by the autolytic disintegration occurring at abortion and intra-uterine foetal death during the last stage of pregnancy. It is likewise possible that the infection heals before the child is born under the influence of the maternal antibodies. Under such conditions the infection is of clinical interest only if it causes a disorder in development—premature birth or malformation. However, if toxoplasmosis is a common cause of these defects, it must be possible to demonstrate more mothers with antibodies in their case than in others.

As is seen in Tables I and II, however, the serological studies did not reveal a significantly large proportion of women with antibodies in any of the selected series. Furthermore, not a single case of toxoplasmosis was found on pathological examination of the dead children or clinical examination of the living ones whose mothers had a high antibody titre. Because of this, I conclude that toxoplasmosis is only rarely a cause of abortion, intra-uterine foetal death, neonatal mortality, premature birth or defective development in the child.

### *Value of Serological Tests and Manner of Antenatal Inception*

Antibodies were observed in the serum of about half the women examined. In view of this it may be reckoned that about 11,500 of the women in the entire series of 23,260 mothers had antibodies. About 700 of these had such a high antibody titre (dye test positive in 1 : 250 dilution or over) that they probably had had an infection within recent years. Nevertheless, only 2 cases of infantile toxoplasmosis were discovered. This shows that it is impossible to draw conclusions regarding diagnosis or prognosis from a single serological test, even in the case of a high titre.

By making repeated tests one can learn to what stage in the antibody curve the case has arrived. A persisting low dye test titre of 1 : 50 or less was found in 45 per cent of the 270 healthy pregnant women in Table II. In these cases the antibodies were probably the result of an infection years ago. A small percentage of the women in Table III showed a persisting high titre. This was apparently caused by a recent infection, past the clinical stage, however. As mentioned before, all these women gave birth to normal children with no signs of toxoplasmosis. Only 1 woman showed serological evidence of fresh infection, but she, too, gave birth to a healthy child. After delivery the child's titre dropped rapidly, indicating that the antibodies were the result of passive immunization. This case of infection with Toxoplasma during pregnancy seems to be the first of its kind to be reported. It shows that the same is true of humans as of monkeys, that the mother can be infected with Toxoplasma during pregnancy without the foetus being infected.

Several authors maintain that the frequent

occurrence of antibodies in pregnant women is due to the lowering of resistance associated with pregnancy and that there is a risk of intra-uterine toxoplasmosis when the mother has a high antibody titre. It has been assumed that the conditions are analogous to those occurring in syphilis in pregnant women. A fact militating against this assumption is that only 2 cases of infantile toxoplasmosis were discovered in the present series, though about 700 women showed a dye test titre of 1 : 250 or more. In my opinion, there is reason to assume that the conditions are the same as in animals. A high antibody titre need not in itself mean that the maternal toxoplasmosis is in an infectious stage. Only in the rare cases where the high titre represents a fresh infection is there a risk of the foetus being infected.

Apart from these exceptional cases, there seems to be no risk of the foetus being infected by Toxoplasma when the mother has a high titre of Toxoplasma-neutralizing antibodies. Instead, the antibodies seem to protect the foetus. For one reason, the antibodies have a strong inhibiting effect on the parasites *in vitro*.

Another is that, judging from the experimental investigations already mentioned, the microbes' prospects of extracellular existence become so small when antibodies begin to appear in the blood that any inflammation soon heals.

For the same reasons there can be no risk of the foetus of a future pregnancy being infected by Toxoplasma, no matter what phase of the infection the mother is in prior to the pregnancy.

On the other hand, there is risk of infection of the foetus during the first 2 weeks of the disease, when the microbes are spread by the blood. This has been shown by a large number of animal experiments, and we may assume that the same is true of humans. How great the risk is, is impossible to say. Judging by experiments on monkeys and the results of this study, it would appear to be of little importance.

*Possibilities of preventing Intra-uterine Toxoplasmosis*

These facts must be taken into account when considering prophylactic measures against intra-uterine toxoplasmosis. The most important measure is to find every case of acute toxoplasmosis among the pregnant mothers. The signs and symptoms of acute toxoplasmosis are often of diffuse nature in the adult, the infection generally resembling those of a common infection. Tender lymph nodes occur in some cases, a rash in others. In the case diagnosed serologically in the present series, the mother showed signs of acute bronchitis. For this reason, it is probably rarely that the disease can be diagnosed clinically. Serological evidence of its presence is not obtained until several tests in succession show a continuous rise in titre. In the meantime there is a chance of the foetus being infected. It seems to be difficult, therefore, to prevent the occurrence of infantile toxoplasmosis antenatally.

*Does Toxoplasmosis justify Termination of Pregnancy?*

There is no need for legally induced abortion because of transplacental passage of toxoplasmosis to the foetus in an earlier pregnancy, since neither among animals nor humans has infection of this kind been observed in two pregnancies in succession. Nor, for reasons just given, is a high antibody titre at the beginning of the pregnancy any justification for its termination.

If fresh toxoplasmosis has been demonstrated, on the other hand, either by discovery of the microbes or a rapidly rising antibody titre, there is obviously a risk of the foetus being infected. Both the animal data and the results of this study would indicate that the risk is insignificant. In view of this fact, it is my opinion that for the time being the pregnancy should be allowed to proceed in these cases. The question cannot be settled until we have more clinical experience.

In every case of this kind in which there is a risk of the foetus being infected, the mother should be treated with sulphapyridine or aureomycin. It may be possible by this means to prevent transplacental infection or favourably affect a foetal infection already present.

In view of what has just been said, there is no reason to advise a woman against another pregnancy because she has borne a child with congenital toxoplasmosis or because she shows a high antibody titre.

## Summary

Two cases of infantile toxoplasmosis were found among 23,260 newborn babies born in Göteborg during a period of 4 years. They are described. No other case was found, despite systematic examination of all the children in the 633 cases of stillbirth or neonatal death and follow-up examination of nearly all the living children during the first year.

Antibodies to Toxoplasma, estimated with the egg and dye test, were found in about 50 per cent of the pregnant women; 3 to 5 per cent of them had a high titre pointing to recent or current toxoplasmosis. Statistical study did not reveal a significantly greater proportion of antibody carriers among the women whose pregnancy resulted in abortion, intra-uterine foetal death, neonatal mortality or a defectively developed child.

Consequently, toxoplasmosis seems to occur rarely among the newborn of Göteborg. The study was likewise unable to prove that toxoplasmosis could cause abortion or intra-uterine death of the foetus, though it did not belie the possibility.

A woman can be infected with toxoplasmosis while she is pregnant without the foetus becoming infected. This was shown by 1 case in which the results of the dye test were negative at the start of the pregnancy but changed to positive in the 4th month with a rapid rise in the titre to a high level.

Antibodies being present in the serum of a large number of completely healthy pregnant women who later bore healthy children, no conclusions as regards diagnosis or prognosis can be drawn from the presence of antibodies, even in high titre. It seems impossible to prevent the occurrence of infantile toxoplasmosis antenatally with the diagnostic possibilities now at hand.

The author is of the opinion that a previous toxoplasmic infection in the mother does not incur any risk for the foetus of a present or future pregnancy. On the contrary, antibodies in the maternal serum probably protect the foetus against toxoplasmosis. The only time when there seems to be risk of the foetus being infected is when a woman without antibodies is infected during pregnancy. It is concluded that as yet toxoplasmosis is not a sufficient indication for the termination of pregnancy.


This study could never have been made had it not been for the friendly co-operation and generous help of a large number of colleagues at the Sahlgrenska Hospital. I am particularly indebted to the following: the gynaecologists, Professor H. Fredrikson, Professor E. Jerlov, and Dr. A. Kjessler; the paediatricians, Drs. Y. Akerrén and K. Holmdahl; the pathologists, Professor J. Mellgren and Dr. S. Olsson; the virologists, Drs. L. Alm, G. von Zeipel, and L. A. Linder; and the ophthalmologist, Dr. S. Holm.

My thanks are also due to a great number of other colleagues, so many that there is not room for them here, as well as to the Göteborg Medical Society and the Board of Directors of the Göteborg City Hospitals for generous financial support.

## References

Adams, F. H. (1948): *Pediatrics*, **2**, 511.

Alm, L. (1948): *Nord. Med.*, **40**, 2109.

Bengtsson, E. (1950): *Cardiologia, Basle*, **17**, 289.

Callahan, W. P., Russell, W. D., and Smith, M. C. (1946): *Medicine*, **25**, 343.

Cowen, D., and Wolf, A. (1945): *J. infect. Dis.*, **77**, 144.

Cowen, D., and Wolf, A. (1950): *J. exp. Med.*, **92**, 393, 413.

Cowen, D., and Wolf, A. (1951): *J. Neuropath. exp. Neurol.*, **10**, 1.

Eichenwald, H. (1948): *Amer. J. Dis. Child.*, **76**, 307.

Farquhar, H. G., and Turner, W. M. L. (1949): *Arch. Dis. Childh.*, **24**, 118.

Frenkel, J. K., and Friedlander, S. (1951): *Toxoplasmosis.* U.S. Public Health Service, Washington. Publ. 141.

Gard, S., Magnusson, J. H., and Hagberg, E. (1952): *Acta paediat.*, **41**, 15.

Gard, S., Magnusson, J. H., Wahlgren, F., and Gille, G. (1949): *Pediatrics*, **4**, 432.

Holmdahl, S. (1949): *Toxoplasmosis and pregnancy.* Elanders, Gothenburg.

Holmdahl, S. (1951): *Acta paediat.*, Suppl. 83, p. 153.

Holmdahl, S. (1952): *Zbl. Gynäk.*, **74**, 1357.

Jacobs, L., and Jones, F. E. (1950): *J. infect. Dis.*, **87**, 78.

Jelke, H. (1950): *Ann. paediat., Basle*, **175**, 434.
Kunert, H., and Jüptner, H. (1952): *Gerbutsh. Frauenheilk.*, **12**, 910.
Macdonald, A. (1949): *Lancet*, **1**, 950.
Macdonald, A. (1950): *Lancet*, **2**, 560.
Paige, B. H., Cowen, D., and Wolf, A. (1942): *Amer. J. Dis. Child.*, **63**, 474.
Parsons, L. G. (1946): *J. Obstet. Gynaec. Brit. Emp.*, **53**, 13.
Piekarski, G. (1950): *Z. Parasitenk.*, **14**, 582.
Plaut, A. (1946): *Amer. J. Path.*, **22**, 427.
Sabin, A. B. (1942), *in* De Sanctis: *Advances in pediatrics*, Vol. I. New York.
Sabin, A. B. (1948), *in* Brenneman: *Practice of pediatrics*. Vol. 4. Hagerstown.
Sabin, A. B., and Feldman, H. A. (1948): *Science*, **108**, 660.
Sabin, A. B., and Feldman, H. A. (1949): *Pediatrics*, **4**, 669.
Thalhammer, O. (1951): *Oest. Z. Kinderheilk.*, **6**, 1.
Tomlinson, W. J. (1945): *Amer. J. clin. Path.*, **15**, 123.
Wolf, A., and Cowen, D. (1939): *Bull. Neurol. Inst., N.Y.*, **6**, 306.
Wolf, A., Cowen, D., and Paige, B. H. (1939): *Amer. J. Path.*, **15**, 657.
Wolf, A., Cowen, D., and Paige, B. H. (1939): *Amer.* **93**, 548.
von Zeipel, G., and Linder, L. A. (1951): *Acta path. microbiol. scand.*, **29**, 222.

# PATERNAL INFLUENCE IN POLYZYGOTIC BIRTHS

## A Family Tree with a Review of the Inheritance of Twinning and the Paternal Mechanisms

BY

A. G. OETTLE

*South African Institute for Medical Research, Johannesburg, South Africa*

IT is now fairly well substantiated that some men are particularly liable to induce multiple conceptions. An example of this ability is presented with a discussion of the inheritance of twinning tendencies. The mechanism of the male influence in polyzygotic births still remains to be demonstrated and consequently many theories have been put forward: these are reviewed in the final part of this paper.

### PART I

### A FAMILY SHOWING A PATERNAL INFLUENCE IN POLYZYGOTIC BIRTHS

The details of this family tree (Fig. 1) were volunteered by Miss F. (III.8), a Staff-nurse at the Johannesburg General Hospital. She died suddenly shortly after the second interview, leaving no relatives in South Africa, and her guardian has not replied to letters asking for addresses of the English relations. The statements of the proposita, therefore, have not been confirmed, but she appeared a highly credible witness, puzzled by the frequency of twinning in her family, yet not appreciating the full significance of what she reported. She stated that the twinning tendency in her family was well recognized in their district while no such tendency was apparent in the families into which they married.

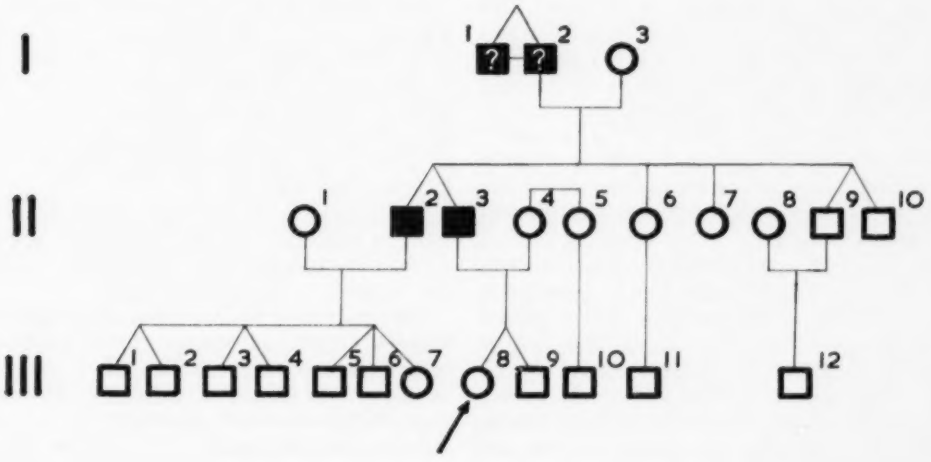



FIG. 1

Family tree of Staff-nurse F. An arrow indicates the proposita III, 8. Those assumed to possess the ability to induce multiple pregnancies are indicated by solid squares or circles. A solid square with a central question mark implies that this interpretation is open to doubt.

### Case Histories

I. 1 and 2. The great uncle and grandfather were identical twins and frequently made use of their likeness in practical jokes.
I. 3. The grandmother gave birth to 2 sets of twins (dizygotic, all male) and 2 single births, both female.
II. 2. Uncle of the proposita. His wife bore 2 sets of dizygotic twins (all male) and 1 of triplets (2 male and 1 female).
II. 3. Father of the proposita. His wife bore 1 set of twins of unlike sex.
II. 5. Maternal aunt who had 1 child.
II. 6. Married with 1 child.
II. 7. Spinster.
II. 9. Married with 1 child.
II. 10. Bachelor.
III. 1–5 all bachelors, killed in the second world war.
III. 6. Unmarried.
III. 7. Married, no issue.
III. 8. Proposita, Staff-nurse F., died of natural causes.
III. 9. Brother of proposita, died in infancy.

### Discussion

1. *Possibility of attributing this occurrence to chance*

Eleven births are recorded in the descendants of I.2, of which 5 were dizygotic twins and 1 a triplet. Since the incidence of dizygotic twin births (in America) is 1:132 (Greulich, 1934) and of triplets 1:7629 (Greulich, 1930), the probability that such a concentration of multiple births would occur in the general population is $1{:}132^5 \times 7629 \div 11$ or $1{:}2.78 \times 10^{13}$. The chances would be somewhat greater than this in a family already chosen as having twins, but none the less it seems legitimate to attribute this occurrence to inherited tendencies.

It, therefore, appears that the dizygotic twin brothers II.2 and II.3 were able to cause polyzygotic births. Furthermore, a similar ability was possessed by either their father I.2 or mother I.3. Since the father was himself a twin, the relatives assumed that he was the spouse responsible for the multiple births in his family, although he himself was an identical twin and the others were fraternal. As identical and fraternal types of twinning tend to be associated in the same pedigree (Southwick, 1939b) it is not improbable that the grandfather I.2 in fact possessed the ability traceable in his sons.

2. *Sex-ratio in the children*

A distinct male preponderance is seen in these dizygotic multiple births, viz, 11 out of 13 children as compared with 2 males out of 4 children resulting from single births. The chances of such an occurrence in a random series are small (1 in 512), but much more evidence is required before this can be regarded as significant. Cory (1895) observed that in four families showing paternal influence in twinning the twins were always of the same sex, but failed to mention what sex and type of twin. Wakley (1895) denied that such twins would always be of the same sex, presenting a family tree clearly demonstrating paternal transmission and yet possessing an unlike pair.

3. *The method of inheritance in the present case*

Since the tendency is rare and appears in 2 successive generations in the absence of consanguinity, this suggests Mendelian dominance. Two of the births in the second generation were single indicating that the gene did not exert its influence equally at every birth (incomplete penetrance).

4. *Other cases showing a paternal influence*

Cory (1895) found in 17 cases of twinning a previous history in the mother's family in 8 and in the father's in 4 cases. In one, twins occurred in both maternal and paternal sides of the family. As regards those which indicated a paternal influence, the twinning relatives were all female, suggesting that the gene could express itself in either sex.

Meyer (1916) concluded that a male influence must be admitted but Bonnevie and Sverdrup (1926) have objected that the mother's family was imperfectly known in his cases.

The pedigrees of Wakley (1895), Peiper (1923), Fetscher (1928) and Sinclair (1940), discussed below, also provide evidence of a paternal influence, as do the population studies of Davenport (1920b) and Southwick (1939b).

In families of parents of fraternities which possessed more than one twin pair, Davenport found an increase in both types of twinning. As regards dizygotic twinning there was an increased frequency in both paternal and maternal families, not only in those of father's,

brother's and mother's sisters but also to a similar extent in those of father's sisters and mother's brothers, which suggests the presence of genes that are uninfluenced by sex.

Southwick (1939b) also produced evidence of an inherited paternal influence, and concluded that the gene must be autosomal.

## PART II

## THE MODE OF INHERITANCE OF THE TENDENCY TO PRODUCE MULTIPLE BIRTHS

As the twinning tendency is sometimes expressed in both sexes (Cory, 1895; Davenport, 1920b; Southwick, 1939b) it is necessary to consider inheritance in both male and female parents. Interpretation of pedigrees may be difficult, so common pitfalls will first be enumerated.

### A. COMMON DIFFICULTIES IN TWINNING STUDIES

1. *Confusion between mono- and polyzygotic births*

Earlier workers do not distinguish different forms of twins e.g., Cory (1895) and Bonnevie and Sverdrup (1926). This omission interferes with detailed interpretation, since the two forms involve totally different mechanisms, and differ in racial incidence and maternal age distribution (Greulich, 1934) although the two types are frequently reported in the same pedigree (Southwick, 1939a, b; Davenport, 1920b). It is not certain that monozygotic twinning is hereditary. Davenport (1920b) found 13 per cent of twin labours (type not stated) in the fraternities of fathers and mothers of monozygotic twins, but Greulich (1934), on the other hand, could not demonstrate more than a very slightly increased frequency of twinning in families of parents of monozygotic twins.

2. *Limited penetrance*

Although the capacity to induce multiple pregnancies may have been inherited, the possessor of this faculty may remain single or have too small a family to reveal the tendency. Furthermore, since polyzygotic births tend to be commoner in older women, contraception will tend to reduce the number of these selectively (Fisher, 1928). Geneticists might regard this as a special case of environmental causes of limited penetrance. Thus, all that can be recognized for genetical purposes is the parent thought to be responsible for actual polyzygotic births, which is not very satisfactory. This, however, is the phenotype.

3. *Sex-limitation*

Another form of reduced penetrance is seen in sex limitation when the twinning gene exerts its effect through an organ peculiar to one sex, and cannot be expressed when present in the opposite sex (e.g., Fig. 8, Bonnevie and Sverdrup, 1926) unless it has some additional action (pleiotropy).

4. *Limited expressivity*

Neugebauer (1913) has pointed out that twin pregnancy may be missed because one sib died shortly after conception and was resorbed during pregnancy. On careful examination of the placenta after a single birth, he was often able to detect evidence of a twin in the form of a foetus papyracus, foetus amorphus, foetus acormus or rudimentary embryonic sac. This occurrence represents an unusual example of limited genetic expressivity, possibly due to sperm or ovum lethals, defects of implantation, placental anastomoses or intra-uterine disease.

5. *Phenocopies*

One can never exclude the possibility in twin pedigrees that a particular polyzygotic birth was not a random occurrence unrelated to the genetic make-up of the parents. This may effectively confuse the interpretation.

6. *Limitations of population and kinship studies*

Valuable as statistical studies have been, they have occasionally led to quite erroneous conclusions. Southwick (1939a), for example, found an increased association between dizygotic and monozygotic twinning in the kinships investigated and concluded that the genes involved must be linked on the same autosome. The correlation of two phenotypes in a population is no proof of linkage, however, since after sufficient generations crossing-over produces completely random distribution of linked genes (Rife, 1939; Snyder, 1951, p. 377). Kinship studies, furthermore, are concerned with a selected population, and abnormal statistics will be obtained with the sibs of the propositi (Cotterman, 1941). Finally,

population studies may be genetically highly misleading if a condition regarded as unifactorial turns out to be due to a multiplicity of different genes.

7. *Multifactorial inheritance*

Early workers tended to write as if twinning were a single mechanism controlled by a single gene. Later writers have been forced to recognize that the subject is more complex. Southwick (1939a and b) distinguished two types of twinning, each being controlled by a single gene. Bonnevie and Sverdrup went further and suggested that in dizygotic twinning three genes might be involved, as they found two exceptions to what they regarded as the usual type of inheritance. The first was the case of a woman who had 8 dizygotic twin births in 13 pregnancies without any history of twinning in her ancestors. (The husband's pedigree unfortunately is not reported!) They concluded, therefore, that this was a character different from and independent of the common tendency to dizygotic twinning, and of the same nature as Davenport's (1919) case (though the latter showed obvious dominant inheritance). As regards their second case, they concluded that by itself it might indicate a sex-linked dominant (p. 150).

The situation is even more complicated. The existence of male influences implies indirect mechanisms for which additional genes are required. Furthermore, the type of multiple birth varies. Some pedigrees produce twins (Wakley, 1895; Taylor, 1931) while others reveal an increased frequency in the higher grades of multiple births, and twins may be rarer than triplets (Grigg, 1890; Davenport, 1919) instead of being 80 times as frequent. It is perhaps significant from the point of view of aetiology that these families occur in cases with female heredity.

Numerous genes must thus be involved in the production of polyzygotic births. This conclusion profoundly affects the method of investigation.

### B. Mode of Inheritance

A variety of different modes of inheritance may be expected, and can be demonstrated in the family trees already published. There are two questions to answer; first, is the inheritance dominant or recessive, and, secondly, what is the situation of the gene on the chromosomes? At present the second question is limited to distinguishing between sex-linked and autosomal characters.

#### Dominant or Recessive?

A. *Dominant traits.* This implies that the character is completely expressed in heterozygotes, but where there is incomplete penetrance, as in multiple births, every possessor of the gene need not exhibit the character. The rule " once lost, lost forever " thus no longer holds.

(a) *Dominant male inheritance.* This would appear to be the common form of inheritance of the male twinning influence. Wakley (1895) described a family where a father and 3 sons had twin families while the father's brother, though having no twin children himself, had twin grandchildren by his son. The type of twin is not distinguished, but the inheritance is dominant with lack of penetrance, and only males are affected.

Peiper (1923) described a family where the father, himself a twin, had 9 sets of dizygotic twin children (all male-female!) The wife remarried and had 6 single births by the second husband. Twins were not known in the families of 9 sisters of the mother. Lenz (1931) not unreasonably doubts the history, which he attributes to mere sensationalism. The chance against 9 successive twins being of unlike sex is about 500 to 1!

A male influence is also indicated in the family tree of quadruplets published by Sinclair (1940). The mode of inheritance is not very obvious but suggests dominance. This pedigree contains a female carrier whose son was father of triplets. The pedigree presented in Fig. 1 would also fall into this group.

(b) *Dominant female influence.* In 1890 Grigg presented a family in which triplets were born in 5 successive generations, with twins in 2 of these. The transmission was on the female line only, the maternal great aunt, aged 90, stating that " her grandmother told her that her grandmother informed her triplets were in the family as far

back as any record could be obtained ". Grigg recorded this striking history with some diffidence, commenting apologetically " I do not suppose that this case possesses any exceptional interest ".

Davenport (1919) described a family in which twins, triplets and quadruplets were produced with 1 single birth only in 4 generations. The inheritance was on the female line and the proposita demonstrated her ability with three husbands, producing twins in the first marriage, 3 twins and 1 triplet in the second, and 3 twins, 4 triplets and 3 quadruplets in the third.

Taylor (1931) also gives a pedigree in which twinning appears in each of 4 generations, with direct female descent. One male parent of twins is present, but it is not known whether he was able to transmit the condition. Bonnevie and Sverdrup (Fig. 8, 1926) give two examples of dominant transmission of a character limited to females and carried by males. Miller (1941) also reports a type of dominance where a generation is occasionally skipped. Female members of his family produced twins, triplets and quadruplets.

It is thus evident that both the male and female influences may be transmitted as dominants, with varying degrees of penetrance.

B. *Recessive inheritance.* This implies that the heterozygote does not display the character, unless the gene happens to be completely sex-linked. Many observers have favoured this mode of inheritance because of the occasional skipping of a generation but, as has been pointed out, poor penetrance and poor expressivity may conceal dominant transmission. The real proof of recessivity is the demonstration of a higher incidence of consanguinity among the parents of the phenotypes than occurs in the general population, and this evidence has yet to be produced.

Suggestive evidence is the occurrence of isolated cases of repeated multiple births in otherwise twin-free pedigrees. Bonnevie and Sverdrup (1923) report 1 such case, while in one of my own (Boatswain B.) 3 pregnancies produced 3 pairs of unlike twins without any precedent in the previous 3 generations of ancestors. In these cases, it is not possible to decide which parent is responsible. Clear evidence for a recessive male inheritance has yet to be produced. Recessive inheritance of the female trait was especially favoured by Bonnevie and Sverdrup in an extensive study of the pedigrees of 4 Norwegian peasant families. Monozygotic twinning could not be distinguished, but the incidence was low and, from the sex-ratios, appears to have represented 11.8 per cent of the total number of twin pregnancies. As twinning could be detected on both sides of the mother's ancestry in most cases, the authors concluded that the mother was a recessive homozygote. Consanguinity was common in the Norwegian valleys investigated, however, so it is quite possible that this apparent inheritance from both sides was coincidental.

### Sex-Linked or Autosomal?

When a gene lies on sex-chromosomes, characteristic modifications of sex ratios are found in phenotypes, from which the gene situation may often be deduced. Sex-limitation will also confine a trait to one sex.

Entirely female or " hologynic " inheritance will result if the gene lies on a pair of attached X-chromosomes since all who receive this gene acquire the chromosome pair that determines femaleness, irrespective of the presence of a Y-chromosome. Grigg's (1890) history is consistent with this possible explanation, but is too incomplete for proof as also is Davenport's (1919) pedigree.

*A. Complete sex-linkage*

(a) *Gene on the non-homologous part of the X-chromosome.* Bonnevie and Sverdrup (1926) suggest a completely sex-linked dominant to explain their Fig. 8, but as mentioned earlier this pedigree could be explained by dominant inheritance with sex limitation, since it lacks male phenotypes, although including two male carriers. No instances of the classical recessive type of sex-linked inheritance are known.

(b) *Gene on the non-homologous part of the Y-chromosome.* A few pedigrees show entirely male transmission (Wakley, 1895, Peiper, 1923) but these are far too short to be acceptable as proof of holandric inheritance. Where penetrance is incomplete it is not necessary for all sons of a

phenotypic individual to be affected, although with complete penetrance this is essential for the diagnosis of Y-chromosomal inheritance.

B. *Partial sex-linkage*

If the gene lies on the homologous part of the sex-chromosome it will tend to cross over from one sex-chromosome to the other, and, depending on whether it predominates on the X- or the Y-chromosome in any one pedigree, it will tend to behave as any similar sex-linked character. Haldane (1936, 1938) showed that in dominant traits the children of affected males will tend to be of like sex as the affected grandparent. In recessive partial sex-linkage, detection requires consanguinity in the parents: the sex of affected children then tends to be that of the father's parent through whom he is related to his wife (Haldane, 1941).

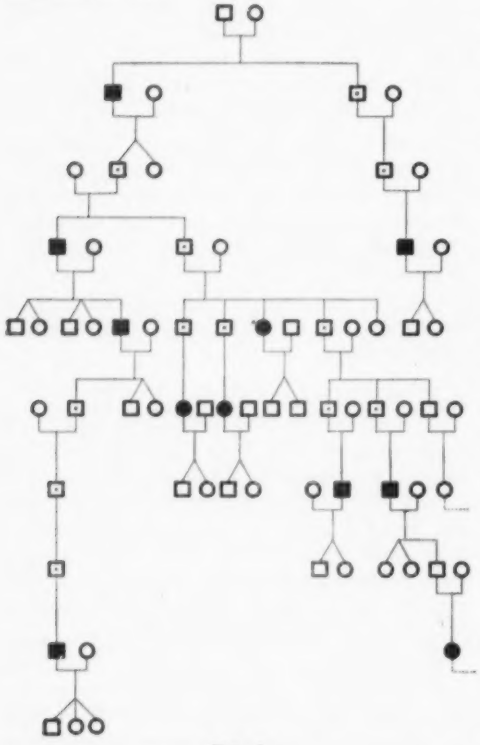


FIG. 2
Portion of Fetscher's family tree, redrawn. A central dot indicates presumed carriers.

In 1928 Fetscher published a remarkable pedigree to demonstrate the male influence in polyzygotic births. He regarded the inheritance as recessive, with which conclusion Gates (1946, p. 926) also agrees. The pedigree, however, can be better explained on the basis of partial sex-linkage. It covers 9 generations, and, if one ignores those who marry into another twinning family, includes 10 pairs of twins and 1 set of triplets. Of these, 9 sets were of unlike sex, and it is likely that the pairs of unlike sex were also polyzygotic (Fetscher, 1928). All but 3 sets of twins were born to males, and transmission was always through males, the lineages extending over 4 to 9 generations. One father of twins had a son (by single birth) who himself was father of twins, which suggests dominant inheritance rather than recessive, contrary to Gates' view, so that the carriers may be regarded as examples of incomplete penetrance. For the most part apparently the gene lay on the homologous part of the Y-chromosome, the 3 female phenotypes representing the result of crossing-over, unless they are phenocopies, which seems unlikely.

## PART III
## MALE TWINNING MECHANISMS

Because the manner in which the father can influence the occurrence of polyzygotic births is far from obvious, and since this possibility has been categorically excluded in the past (Bonnevie and Sverdrup, 1926), it may be profitable to examine the processes involved in polyzygotic births to indicate where this influence might be exerted. Most of the evidence depends on studies of twinning, from which the mechanisms affecting the wider field may be deduced.

A. *The processes involved in dizygotic twinning*

1. *Proven mechanisms*

Fertilization of two eggs generally necessitates the rupture of two separate follicles and consequently two corpora lutea are usually found, occasionally both in the same ovary. On rare occasions, however, only a single corpus luteum is present. This has given rise to considerable speculation, but as binovular and polyovular follicles are known to occur

(Strassman, 1908; Arnold, 1912) the existence of a single corpus luteum in association with dizygotic twins can be explained without difficulty.

2. *A third type of twin*

Many workers have suggested the existence of a third type of twinning to account for the occurrence of dizygotic twins whose resemblance is much closer than would be expected of litter mates. This postulate seemed to be confirmed by certain surveys which failed to reveal a clear line of differentiation between mono- and dizygotic twins (Thorndike, 1905; Fisher, 1919). In more recent studies, however, it has not been necessary to depart from the two generally accepted classes, though Newman, Freeman and Holzinger (1937) admit that they found " some overlap between the two groups, so that a composite index of physical measures alone is not sufficient to differentiate between the two classes of twins " (p. 351).

An intermediate group, if it exists, will comprise either dissimilar monozygotic twins or similar dizygotic twins.

A. *Dissimilar monozygotic twins*

Newman (1931) has pointed out that late cleavage of the germinal disc would tend to produce dissimilarity in monozygotic twins, as can frequently be seen in conjoined twins. One author has gone so far as to suggest that sex reversal might occur and monozygotic twins be of different sex (Levin, 1931)! He based this suggestion on a case of mirror-imaging in twins of opposite sex. A brown sector was present in the right iris of a man who stated that his deceased twin sister had shown the same abnormality in her left eye. As no other evidence of similarity was adduced, it seems far more probable that in this case undue weight has been given to mirror-imaging as proof of monozygosity, and that this is an example of dizygotic twinning. At least one form of mirror-imaging (left handedness) is known to occur with equal frequency in both forms of twins (Rife, 1941).

B. *Similar dizygotic twins*

Dizygotic twinning apparently provides the bulk of the intermediate group. In one series of 500 twin pairs the 5 doubtful cases all turned out to be cases of fraternal twinning (Rife, 1941), which strengthens the view that unnatural similarity may sometimes occur in a dizygotic pair. Such resemblance has been explained on the grounds that one pair of gametes was more closely related than normal; the presence of this relationship is the basis of the so-called " third type of twinning ". Two possibilities have been considered in the literature.

(i) *Premature cleavage of the ovum*

Danforth (1916) and Fisher (1919) both suggested that an ovum might divide after maturation and the two cells so formed be fertilized by two separate sperms. The two nuclei from this division of the ovum would be identical. Danforth based this suggestion on current work on sea-urchins and bees where penetration of a sperm sometimes initiates premature cleavage; one haploid cell is fertilized and the other then develops parthenogenetically.

(ii) *Fertilization of a polar body*

Curtius (1927) suggested that the second polar body (or a larger cell corresponding to it) might be fertilized. The second polar body was at that time thought to be genetically identical with the ovum, but since chromatid exchanges (crossing-over) are now known to occur before the first meiotic division this identity holds only for those parts of the chromosome in which the second meiotic division is equational.

(iii) *Spermatozoal similarity*

A third possibility seems to have been ignored, though it postulates no new mechanisms whatsoever, viz., that the eggs are different and the spermatozoa related, being derived from the 4 spermatozoa developing from a single spermatocyte. Such spermatozoa have certain chromosome regions in common, though two have X- and two have Y-chromosomes. The chance that two such related spermatozoa will fertilize both eggs is remote, but this is the only explanation which is confined to known physiological mechanisms.

B. *Possible mechanisms of the male influence in dizygotic twinning.*

1. *Induction of additional female gametes.*

Gates (1946, p. 925) has suggested that vigour

of coitus might cause rupture of two follicles, though this is naturally not presented as a factor in an inherited tendency. If such traumatic rupture is possible, one would imagine that it would cause sufficient dyspareunia to render this paternal faculty self-limiting.

Guttmacher (1939) thought that the male influence in twinning might be due to an hereditary capacity to fertilize polar bodies. This ought to be easily recognizable as it involves the third type of twinning, which has not yet been reported. There is thus no evidence that the male can induce the formation of additional female gametes, and other explanations of the male influence must be found.

2. *Increased ability to employ naturally occurring polyovulation*

Neugebauer (1913) stated that a large number of twin pregnancies tended to pass unrecognized because 1 foetus died *in utero*, consequently twin pregnancy occurs more frequently than twin births. Davenport (1920a) also concluded that in humans double ovulation occurred more frequently than twinning, since counts of corpora lutea in ovaries of pregnant and non-pregnant women reveal a frequency of double ovulation greater than that of twin-births. In one investigation of 33 sets of ovaries the number of corpora lutea and follicles about to burst [sic!] indicated a 15 per cent incidence of double ovulation—20 times that of dizygotic twinning! Unfortunately he does not give the proportion of follicles about to burst, which is regrettable since ripe follicles may involute at the eleventh hour and their presence cannot be taken as proof of ovulation. Davenport also states in this paper that " there is evidence based upon counts that have been made on the corpora lutea of non-pregnant and pregnant women that the rate of occurrence of 2.3 corpora lutea in the ovary is much greater than the occurrence of twins ". A rate of double ovulation of 2.3 per cent is 3 times as high as the rate of binovular twin births, and this seems much more likely to be accurate than the figure based on corpora lutea and ripe follicles.

On the other hand, Bonnevie and Sverdrup (1926) could not find evidence of lack of correspondence between the frequency of polyovulation and twinning in a " long series of investigations of the ovaries of pregnant women." They point out that, although discrepancies between the number of ovulations and of conceptions occur in animals with a high incidence of multiple births, scarcely any such deviation was detected in cattle, where the twinning incidence is 0.4 per cent. By analogy, since the twinning incidence in humans is also relatively low, they expected to find close correspondence here also. The comparison between man and bovine is hardly fair, however, since a paternal influence in dizygotic twin births is known to occur in humans but as far as I am aware has not yet been demonstrated in cattle, where it should be easily detectable.

Those who recognize the male influence will be loth to discard Neugebauer and Davenport's conclusions. Assuming that normally there are limiting factors which reduce the frequency of fertilization of both ova or the chance of both reaching maturity, increased chance of fertilization or survival will tend to increase the frequency of multiple births, without any increase in polyovulation. On this assumption the male influence can be explained quite simply.

A. *Freedom from lethal factors*

Davenport (1920a, 1927) suggested that normally many ova are prevented from completing their development by lethal factors in the sperm. It is recognized that about 1 in 5 fertilized ova does not complete its development, but this does not explain the difference between Davenport's figures for the incidence of polyovulation and that for dizygotic twinning, unless these lethal factors are limited to multiple pregnancies. This will happen if these influences are facilitated by factors like uterine overcrowding and placental anastomoses which militate specifically against the intra-uterine survival of twins. Until more is known about lethal factors it will not be possible to assess what part they play.

B. *Absence of zygote-produced inhibitors of fertilization or implantation*

In 1931 Lenz suggested that the zygote might produce substances which inhibit fertilization

of other ova. I know of no evidence that such substances exist.

Southwick (1939b) has suggested that in man the gene for dizygotic twinning, whether it come from father or mother, might affect the zygote so as to extend the receptive state of the uterus. It is not certain whether uterine receptiveness is a limiting factor in man although in certain species multiple fertilized ova compete for the implantation site. Thus in the jumping shrew, *Elephantulus myurus jamesoni*, about 120 ova are liberated in one menstrual cycle, and on account of uterine anatomy only 2 can implant (van der Horst and Gillman, 1941).

C. *Increased duration of fertility in the sperm*

In human matings it is well known that some degree of coincidence of insemination and ovulation is essential for fertilization to occur. Moreover, the fertile life of the sperm is probably considerably less than the motile life (Van Drimmelen and Oettle, 1950). Similarly the fertile life of the ovum is limited. Since one ovulation tends to inhibit the rupture of other ripe follicles, polyovulation in the human female probably implies that the follicles have ruptured within a short time of one another before inhibitory processes can become effective. In most cases, therefore, fertilization of 2 ova probably results from a single coitus. This may explain why evidence for superfecundation is so difficult to produce in humans, though the possibility obviously can never be excluded.

Davenport (1920a) suggested that the male who is prone to father twins is better able to fertilize all the available ova. A simple explanation for such an ability is an inherited prolongation of the period of fertility in the spermatozoa. The incidence of binovular twinning would then tend to approximate that of double ovulation. Males possessing this ability would not display it at every conception, but only when double ovulation approximately coincided with insemination.

More facts are necessary, however, before this suggestion can be accepted. The immediate requirement is a reliable estimate of the frequency of double ovulation and double impregnation in women of different age groups. Without this, any statements regarding the physiological factors responsible for polyzygotic births will remain a matter of opinion.

As regards cases like that of Brattström (1914), where a Russian peasant is claimed to have induced 35 successive multiple births, if the data are reliable, some other mechanism will have to be sought, such as the ability to fertilize polar bodies postulated by Curtius (1927).

*Comparison with possible female influences in multiple births*

In addition to common factors like freedom from lethals and increased duration of fertility, there are others peculiar to the female, like binovular and polyovular follicles, frequency and simultaneity of polyovulation, receptivity of the uterus, and type of ovum liberated. Polyovular follicles might explain the tendency of female twinning lines to produce the higher degrees of polyzygotic births. Davenport (1927) found the incidence of twinning female lines is equal to or greater than that of male lines, as would be expected if the possible mechanisms for increasing the number of multiple births are more numerous and varied in females.

## Summary and Conclusions

A pedigree is presented in which certain males appear to have been able to induce a high incidence of polyzygotic births. Previous cases in the literature confirm the existence of this masculine ability, which is inherited as a Mendelian dominant of incomplete penetrance. The inheritance of male and female tendencies to polyzygotic multiple births is more complex than previously imagined, and the difficulties of its investigation are unusually numerous. Most types appear to be dominant, but recessives are known. Many factors are involved, and many types of inheritance may be expected. One published pedigree has been re-examined and appears to demonstrate partial sex-linkage, i.e., that most of the time the gene lay on the homologous part of the Y-chromosome.

The origins of polyzygotic pregnancies are considered, and it is suggested that abnormally similar dizygotic twins may arise as a result of spermatozoal relationship. Of numerous theories, prolongation of the fertile life of

ejaculated spermatozoa appears the simplest explanation of the male influence in twinning. This assumes that polyovulation occurs more frequently than multiple pregnancies.

## References


Arnold, L. (1912): *Anat. Rec.*, **6**, 413.

Bonnevie, K., and Sverdrup, A. (1926): *J. Genet.*, **16**, 125.

Brattström, E. (1914). Quoted by Gates (1946).

Cotterman, C. W. (1941): *Sci. Mon. N.Y.*, **53**, 227.

Cory, R. (1895): *Lancet*, **2**, 1105.

Curtius, F. (1927): *Z. KonstLehre*, **13**, 286. Quoted by Greulich (1934).

Danforth, C. H. (1916): *J. Hered.*, **7**, 195.

Davenport, C. B. (1919): *J. Hered.*, **10**, 382.

Davenport, C. B. (1920a): *Proc. Soc. exp. Biol. N.Y.*, **17**, 75.

Davenport, C. B. (1920b): *Amer. Nat.*, **54**, 122.

Davenport, C. B. (1927): *Z. indukt. Abstamm.—u. VererbLehre*, **46**, 85.

Fetscher, R. (1928): *Arch. Rass.—u. Ges Biol.*, **20**, 432.

Fisher, R. A. (1919): *Genetics*, **4**, 489.

Fisher, R. A. (1928): *Proc. roy. Soc. Lond., B.* **102**, 286.

Gates, R. R. (1946): *Human genetics.* Macmillan. New York.

Greulich, W. W. (1930): *Amer. Nat.*, **64**, 142.

Greulich, W. W. (1934): *Amer. J. phys. Anthrop.*, **19**, 391.

Grigg, W. C. (1890): *Brit. med. J.*, **1**, 541.

Guttmacher, A. F. (1939): *Med. Clin. N. Amer.*, **23**, 427.

Haldane, J. B. S. (1936): *Ann. Eugen.*, **7**, 28.

Haldane, J. B. S. (1938): *Lancet*, **2**, 1449.

Haldane, J. B. S. (1941): *J. Genet.*, **41**, 141.

Lenz, F. (1934). *in* Baur, E., Fischer, E., and Lenz, F.: *Human heredity.* Allen & Unwin. London. p. 734.

Levin, M. (1931): *J. Hered.*, **22**, 17.

Meier, A. (1951): *Ähnlichkeitsdiagnose bei* 100 *gleichgeschlechtlichen Zwillingspaaren.* M. D. Thesis. University of Basle.

Meyer, H. (1916). Quoted by Bonnevie and Sverdrup (1926).

Miller, R. E. (1941): *Anat. Rec.*, **80**, 411.

Neugebauer, F. V. (1913): *Zbl. Gynäk.*, **37**, 1061.

Newman, H. H. (1931): *J. Hered.*, **22**, 201.

Newman, H. H., Freeman, F. N., and Holzinger, K. J. 1937): *Twins: a study of heredity and environment.* University Press. Chicago.

Peiper, A. (1923): *Klin. Wschr.*, **2**, 1651.

Rife, D. C. (1939): *Human Biol.*, **11**, 546.

Rife, D. C. (1941): *Sci. Mon. N.Y.*, **53**, 148.

Sinclair, J. G. (1940): *J. Hered.*, **31**, 163.

Snyder, L. H. (1951): *in* Dunn, L. C. (ed.): *Genetics in the 20th century.* Macmillan. London. p. 376.

Southwick, W. E. (1939a): *Amer. Nat.*, **73**, 44.

Southwick, W. E. (1939b): *Human Biol.*, **11**, 179.

Strassman, P. (1908): *Z. Ethn.*, **40**, 362.

Taylor, C. E. (1931): *Brit. med. J.*, **2**, 384.

Thorndike, E. L. (1905): *Arch. Phil. Psychol. sci. Meth.*, **1**, 64.

Van der Horst, C. J., and Gillman, J. (1941): *Anat. Rec.*, **80**, 443.

Van Drimmelen, G. C., and Oettle, A. G. (1950): *Proc. Soc. Stud. Fertil.*, **1**, 6.

Wakley, T. (1895): *Lancet*, **2**, 1289.

# HYPERGLYCAEMIA AND HAEMORRHAGIC SHOCK IN PREGNANCY

## Preliminary Study

BY

ROBIN MURDOCH, M.B., M.R.C.O.G.

*From the Research Department, Glasgow Royal Maternity and Women's Hospital*

FROM the clinical appearance of a patient in profound shock, it is obvious that marked metabolic changes are occurring or have occurred. When one considers the principal signs such as the pale or ashen-grey, cold, clammy skin, the rapid, thready or imperceptible pulse, the restlessness or apathy, the lustreless eyes, irregular respirations, and greatly reduced or even unrecordable blood-pressure, it is a matter of wonder that complete recovery may take place in a short time with the aid of the appropriate therapy. But the longer the patient remains in this shocked state, the greater are the changes in metabolism to be expected. It is obvious that these metabolic changes are of importance both for the understanding of the process of shock and for the formulation of a rational and specific mode of therapy.

Metabolic changes in shock have been the subject of study of many workers. The studies of Beecher (1949) and Wiggers (1950) are among the more recent in relation to shock in the human subject. A greater volume of work has been reported in relation to experimental shock in animals by Nishi (1909), Slocum and Lightbody (1931), Robertson (1935), Engel, Winton and Long (1943), Clark and Rossiter (1944), and Frank, Seligman and Fine (1946). All of these studies, however, have been made on the non-pregnant subject and particularly in relation to traumatic shock. No similar study has been made of shock in the pregnant subject in whom the main aetiological factor is haemorrhage.

The present communication deals with the changes in blood-glucose values during the initial stages and throughout the subsequent phases of the shock syndrome in pregnant women even to the extent of irreversibility.

*Method*

The method adopted was to take a sample of blood from one of the arm veins when it was necessary to start a saline, plasma or blood transfusion. It was therefore taken usually at the height of the shock and before any treatment had been instituted. Some of the sample blood was required for grouping and cross-matching and the remainder was put into a tube containing fluoride and thoroughly shaken. The blood sugar was estimated by the Herbert and Bourne (1930) colorimetric method and recorded in mg. per cent.

In the later cases further samples were taken when there were obvious signs of recovery from the shock, in order to find the effect of treatment. Fasting specimens were examined on subsequent days.

Altogether 40 cases were studied. They formed four groups according to the cause of haemorrhage. Group I consisted of 22 cases of post-partum haemorrhage; Group II contained 7 cases of accidental haemorrhage. Haemorrhage from abortion in 8 cases accounted for Group III, and intraperitoneal haemorrhage from rupture of the uterus was the cause of shock in Group IV, composed of 3 cases. No attempt was made to group the patients according to the degree of shock nor to assess the amount of blood loss, especially as in the majority the haemorrhage had occurred before admission. However, it was possible in these 40 cases to fix the time of the onset of the shock reasonably accurately.

Nearly all cases with the exception of some in the accidental haemorrhage group exhibited most of the cardinal signs of shock mentioned earlier.

*Blood-sugar Changes*

The average blood-sugar value in these 40 cases, irrespective of cause or duration of shock, was 222 mg. per cent with a range of 110 mg. per cent to 364 mg. per cent. Preliminary analysis of these figures revealed one important point. Shock of short duration produced little change in the blood-sugar level and it was only after the shock phase had lasted for approximately 30 minutes that an appreciable rise in blood-sugar levels was noted. In 5 of these cases blood transfusion was given within 10–15 minutes of the development of the shocked state and a satisfactory response was rapidly produced.

The cause of haemorrhage was abortion in 2 cases, retained placenta in 2 cases and accidental haemorrhage in 1 case. The highest blood-sugar value in this small group was 172 mg. per cent and the lowest was 110 mg. per cent. The direct relationship between the duration of shock and the level of the blood-sugar is clearly demonstrated in Fig. 1.

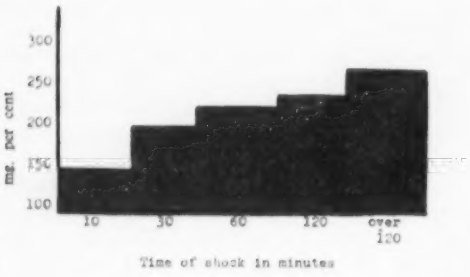



FIG. 1

A further analysis was made to determine whether the blood-sugar level was related to or modified by the cause of haemorrhage. Accordingly the cases were arranged in their four groups, namely, postpartum haemorrhage, accidental haemorrhage, abortion haemorrhage, and intra-peritoneal haemorrhage.

*Postpartum Haemorrhage*

This group consisted of 22 cases, all of whom suffered from haemorrhage during or immediately after the third stage of labour. The degree of shock was severe in most cases. The highest systolic blood-pressure was 90 mm.Hg and the highest diastolic reading 60 mm.Hg, but the average reading was 70 mm.Hg systolic and 43 mm.Hg diastolic. There were, however, 3 cases in whom neither reading was obtainable. No direct relationship could be found between level of blood-sugar and either reading nor was there any apparent relationship between pulse pressure and blood-sugar. A time relationship was the only positive finding, the blood-sugar rising with the duration of shock in a manner similar to that for the whole series (Fig. 2). This group differed in one particular respect from the other groups. All of these patients had completed their labour and by virtue of this it might be thought that some relationship might exist between the length of labour and the degree of shock, and therefore so affect the change in blood-sugar values.

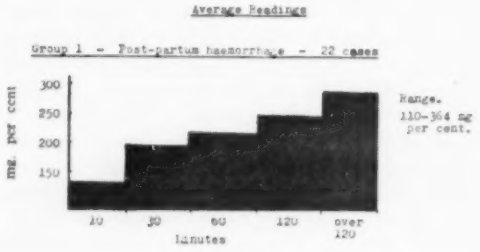



FIG. 2

The length of labour in each case was estimated where possible. This varied from 2 hours to 50 hours with an average of 19 hours but no relationship was to be found between the blood-sugar reading and the duration of labour, e.g., the patient who was in the shocked state for only 5 minutes, with a blood sugar of 157 mg. per cent, had had a labour lasting 30½ hours and one on the 2-hour shock group with a blood sugar of 236 mg. per cent had a short labour of 2 hours. Despite the fact that there was apparently no connexion between blood-sugar level and labour, it was decided to select some normal cases and follow them through labour, taking samples of blood at different stages. In order to prevent any apparently false readings and impressions, none of these patients was given glucose in any form during labour.

Nine normal cases selected at random, 4

primigravidae and 5 multiparae, were admitted to the labour ward with pains established and with the cervical os from 1 to 3 fingers dilated. In some cases as many as 3 samples were taken in the 1st stage: one preferably at its completion; another at crowning of the head or immediately after delivery; another after the 3rd stage was completed; and a fasting specimen on the following morning. In 3 of the cases a sample was taken 2 hours after completion of the 3rd stage. In all cases labour was normal and delivery spontaneous. Fig. 3 has been compiled by taking the average of all readings at the different stages. It will be seen that there was a gradual rise in the blood-sugar level from 125 mg. per cent in the 1st stage to 145 mg. per cent just after the 3rd stage.

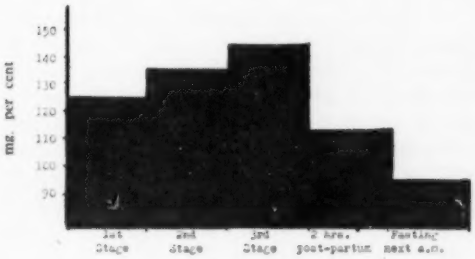



FIG. 3

Analysis of individual cases showed that the increase in blood sugar in most cases commenced in the 2nd stage and continued throughout the 3rd stage of labour. In 2 cases, however, the rise was delayed until the 3rd stage. It can be seen from Fig. 3 that, although there is a moderate increase in the blood sugar during labour, the levels reached are not comparable with those recorded where shock has been present for 30 minutes and more.

*Accidental Haemorrhage*

This group consisted of 7 cases, 5 of which were of the mixed accidental type, 1 of the concealed type, and 1 of the revealed type. Shock was particularly severe in 2 cases who were unconscious on admission. The highest systolic blood-pressure was 130 mm.Hg and the highest diastolic reading was 85 mm.Hg; the lowest systolic reading was 85 mm.Hg and the lowest diastolic reading was 40 mm.Hg, the average systolic reading being 105 mm.Hg and the average diastolic 65 mm.Hg. The highest pulse pressure recorded was 50 mm. and the lowest 27 mm. The only feature noted was that the highest blood-sugar reading occurred in one of the cases who was unconscious and had the lowest pulse pressure. The weight of retroplacental clot varied from 1 pound 2 ounces to 1 pound 12 ounces, but no relationship between blood-sugar reading and weight of clot or type of haemorrhage (concealed or mixed) was evident. Four of the 7 cases received a blood transfusion, but the other 3 recovered with shock treatment other than intravenous infusion. Labour was induced in all cases following recovery from shock, so, since all the blood-sugar readings were taken at the height of shock, the length of labour is not significant. The time-shock relationship was again a positive finding, and the blood-sugar reading increased as the shock time increased but at lower levels than in the P.P.H. group (see Fig. 4). This will be considered in the discussion.

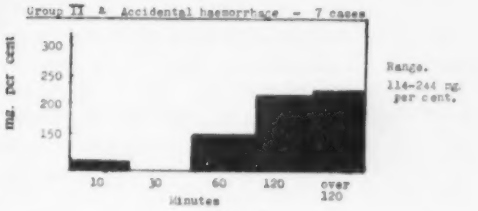



FIG. 4

*Abortion*

This group consisted of 8 cases in whom the duration of pregnancy varied from 6 weeks to 22 weeks. Haemorrhage was severe in 4 cases, 3 of whom had been shocked up to 2 hours. The highest systolic blood-pressure was 115 mm.Hg and the highest diastolic reading 80 mm.Hg, the average systolic being 100 mm.Hg and the average diastolic 66 mm.Hg. In one case the blood-pressure was not recordable. On the basis of the classification of shock according to blood-pressure readings suggested by Wiggers, these cases would not appear to be so collapsed as those in the postpartum or intra-peritoneal

group The blood-sugar level increased from 167 mg. per cent in the 10-minutes shock group to 240 mg. per cent in the 1-hour and 2-hour group. This was the only type of haemorrhage where the average did not rise when the time of shock exceeded 1 hour. No connexion was evident between the duration of the pregnancy and the blood-sugar reading.

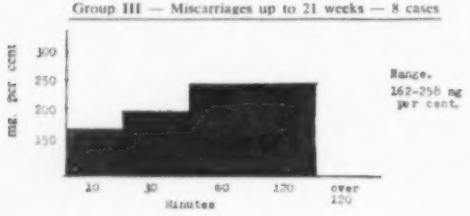



FIG. 5

In 2 of the cases the shock time was less than 10 minutes before treatment was commenced and these gave the lowest blood-sugar readings.

*Intra-peritoneal Bleeding*

There were 3 cases in this group, 2 being cases of ruptured uterus (previous Caesarean section) and 1 a rupture of a rudimentary horn. All 3 were in the shocked state for long periods, 1 for nearly two hours, and the remaining 2 cases for 3 and 5 hours respectively. The blood-glucose levels ranged from 233 mg. per cent to 340 mg. per cent, the average being 281 mg. per cent. In the case with the highest reading of 340 mg. per cent shock had been present for 5 hours and there was a very considerable quantity of blood in the peritoneal cavity. After the patient had recovered from shock and the operation of hysterectomy, the blood-glucose level had fallen to 210 mg. per cent. The fasting blood glucose

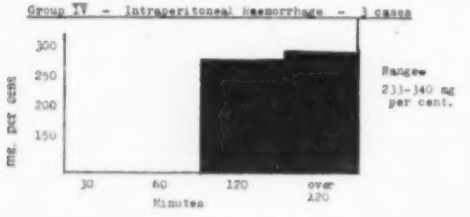



FIG. 6

on the 3rd day of the puerperium was 175 mg. per cent and on the 5th day 146 mg. per cent. Further reference will be made to this later in the paper.

In the above-mentioned cases the highest systolic blood-pressure reading was 90 mm.Hg and the highest diastolic 60 mm.Hg, the average reading being 78 mm.Hg systolic and 55 mm.Hg diastolic. These readings approximated to those found in the postpartum haemorrhage group.

Again the only positive finding was that the blood-sugar levels increased with the duration of the shock.

There also appeared to be a direct relationship between the blood-sugar levels and the amount of blood lost, but the series is too small to allow a statistical evaluation.

*Influence of Blood Transfusion Therapy*

In 12 of the cases (6 suffering from postpartum haemorrhage, 3 from accidental haemorrhage, 2 from abortion, and 1 from ruptured uterus) the effects of treatment were noted with regard to the blood-sugar readings (Table I). These were taken at the completion of the transfusion and/or when there was recovery from shock. In 8 of the cases, fasting specimens were taken on one or two days of the puerperium. The times which elapsed between the initial, or shock, blood sugar and the recovery or improvement level are shown in column 8 of the table, but they do not appear to bear any direct relationship to the percentage fall in the blood-sugar values, It was noted that in Case 9, where the patient had a second collapse, the fall in blood-sugar value was less steep and continued over a longer period, the pulse rate remaining at 100/minute for the first 5 days of the puerperium. In Case 11, where there was also a second collapse, the blood sugar rose to a higher level than the first collapse reading and had only fallen to 184 mg. per cent on the 4th day of the puerperium. The pulse rate in this case remained at 120/minute for the first 3 days of the puerperium. On the 7th day the blood sugar had fallen to 128 mg. per cent. The return of the blood sugar to normal levels may be affected by a second collapse, despite treatment, or by the degree of shock, taking the initial blood-sugar reading as an indication.

TABLE I

| Case | Type (1) | Time of shock (hours) (2) | Blood-sugar readings (mg. per cent) | | | | Percentage fall (7) | Recovery time (hours) (8) | Subsequent blood-sugar fasting levels (9) | | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Shocked (3) | At recovery or Improvement (4) | 2nd shock (5) | At recovery (6) | | | | | |
| 1 | P.P.H. | >2 | 238 | 131 | — | — | 45 | 8¼ | — | — | — |
| 2 | P.P.H. | 1 | 272 | 152 | — | — | 44 | 5 | 126 | | — |
| 3 | P.P.H. | 2 | 298 | 170 | — | — | 43 | 3½ | 1st day 168 | 2nd day 158 | — |
| 4 | Ruptured uterus | >2 | 340 | 210 | — | — | 38 | 4 | 3rd day 175 | 5th day 146 | — |
| 5 | Accid. Haem. | 1 | 148 | 98 | — | — | 34 | 12 | 1st day 84 | 2nd day 76 | — |
| 6 | Abortion | 2 | 238 | 162 | — | — | 32 | 6 | — | — | — |
| 7 | P.P.H. | >2 | 284 | 204 | — | — | 28 | — | — | 2nd day 120 | — |
| 8 | Abortion | 1 | 240 | 183 | — | — | 23.7 | 15 | 1st day 152 | — | — |
| 9 | Accid. Haem. | 2 | 204 | 165 | 204 | 183 | 19<br>10 | 2<br>4½ | —<br>— | —<br>— | Pulse rate 120/mm. for 3 days. |
| 10 | P.P.H. | ½ | 170 | 120 | — | — | 29 | 3½ | — | — | — |
| 11 | P.P.H. | >2 | 219 | 204 | —<br>230 | —<br>? | 6.8 | 3½ | 4th day 184 | 7th day 128 | Pulse rate 120/mm. for 3 days. |
| 12 | Accid. Haem | ½ | 114 | — | — | — | — | — | 1st day 96 | 2nd day 78 | — |

## Discussion

From the preceding data it is established that hyperglycaemia occurs in varying degree in the pregnant woman suffering from haemorrhagic shock. This agrees with the findings of Wiggers, and of Beecher who made his observations in wounded soldiers at the battle-front.

On a time-relationship basis two definite points were noted on studying the results.

(*a*) It was evident from the table showing the levels of the blood sugar compared with the length of shock that up to 15 minutes in shock there was no appreciable rise in the blood sugar.

(*b*) When shock had been present for 30 minutes a significant rise in the blood-sugar level occurred. The level increased as the time of shock increased and reached the highest level recorded (364 mg. per cent) in the one fatal case of the series. In that case the sample was taken 1 hour before death when the patient was in profound and obviously irreversible shock. This finding does not agree with Wiggers who has stated that there is a terminal hypoglycaemia.

It is obvious when the last two columns in each group are compared that the blood-sugar levels in the cases of accidental haemorrhage are much lower. This diminished blood-sugar response may indicate that the glycogen store in the liver is diminished in toxaemic cases. This would agree with Govan's findings (personal communication) that the response to adrenalin is diminished in toxaemia of pregnancy and may be correlated with the results of tissue-fluid examination in similar cases (Mukherjee and Govan, 1950). All of these findings indicate that there is probably an upset of carbohydrate metabolism in toxaemia.

There did not appear to be any definite relationship with any other factor such as length of labour, duration of pregnancy, blood-pressure or pulse-pressure. Nevertheless, it was noted that these last two were higher in the abortions and accidental haemorrhage group than in the postpartum haemorrhage group, whereas the blood-sugar levels were not so high.

Although the cause of shock in these cases (i.e., haemorrhage) had ceased to operate, the blood sugar was maintained at a high level as long as the patient remained in a shocked condition. This may last for several hours, the longest in this series of cases being 5 hours. This agrees with Taylor *et al.* (1944), who observed a steady rise in blood-sugar levels in patients admitted with thermal burns. Beecher (1949) also noted that in wounded soldiers the blood sugar appeared to rise significantly both with increase in the severity of the shock and with increase in blood loss.

The normal response to adrenalin hyperglycaemia is a production of insulin which returns the blood sugar to normal and, as this does not occur in haemorrhagic shock, several possible reasons can be advanced to explain it. (*a*) A lack of or a decreased production of insulin—there is no evidence of this. (*b*) Insulin antagonists are at work—it is known that these antagonists belong to the pituitary adrenal system (Selye, 1950) and this would agree with the findings of Fraser, Albright and Smith (1941) in relation to nitrogen metabolism in shock. This would also fit in with the results of Slocum and Lightbody (1931) and Clark and Rossiter (1944). (*c*) The function of the liver is affected by anoxia in that the rate of deposition of sugar in the liver may be slowed down (Frank, Seligman and Fine, 1946). As the anoxia of the liver increases so does the glycogenic function cease, until the irreversible state is reached. While this may be the position in the terminal stages of shock, it seems unlikely that it could operate throughout shock. It therefore seems probable that in the earlier phases the maintenance of the blood sugar is due to the action of insulin antagonists.

### *Source and Utilization of Glucose in Shock*

The question of the source or sources of the blood sugar is still a matter for conjecture but the following possibilities are presented.

(*a*) The major and immediate source is probably liver glycogen, as evidenced by Robertson (1935). In experiments on cats following haemorrhage, he showed that there was a much more rapid rise in the sugar content of hepatic vein blood than in that of heart blood. This indicates that there is a production of extra glucose from the liver.

(*b*) The stimulus to production of sugar is most probably adrenalin. Engel, Winton and Long (1943) came to this conclusion following

their experiments on rats. They produced haemorrhagic shock in rats previously fed on high protein diet to give a high liver-glycogen level, and found that a hyperglycaemia was present. In those rats where the initial liver-glycogen level was low, hyperglycaemia was completely or largely abolished.

In a series of tests made personally on pregnant women at various stages, it was found that adrenalin produced a significant rise in the blood-sugar level 15–30 minutes after injection. It was only after the lapse of a similar time that a significant increase in the blood sugar was noted in shocked patients.

On the other hand, several authors have conducted experiments on animals to show that, even if the adrenals are removed or destroyed, hyperglycaemia can still occur. It was found by Slocum and Lightbody (1931) that adrenalectomy did not prevent hyperglycaemia in burned rabbits. Clark and Rossiter (1944) made a similar observation, while Nishi (1909) noted that an increase in the blood-sugar level could follow destruction of both adrenals. Therefore hyperglycaemia is not altogether due to adrenalin.

Another possible source of increase in the blood-sugar level has been suggested by Selye (1950), who states that there is an increased transformation of protein into sugar by the action of the anterior pituitary-adrenal system. This could be correlated with what has been stated in regard to the action of insulin antagonists in maintaining the blood sugar.

To summarize, it is probable that the initial rise in blood sugar occurring after 15–30 minutes is due to the action of adrenalin on the liver glycogen but subsequently the blood sugar is maintained at a high level through the action of the pituitary-adrenal system. It seems unlikely that utilization is normal in view of the obvious depression of metabolism in shock. Taylor, Levenson and Adams (1944), however, found a moderate increase in metabolic rate in a few cases in their study. Such a conclusion would not be consistent with the findings in this group, but the explanation may lie in the fact that very few of Taylor's cases showed evidence of shock whereas all the cases in the present series were definitely shocked. Wiggers and Beecher found an increase in organic-acid excretion which suggests an inability to metabolize carbohydrate. Taylor *et al.* report that when glucose was administered intravenously the hyperglycaemia was not significantly increased and in some cases was diminished after a period of 2 hours. On the basis of these findings they have claimed that the added glucose was metabolized. It appears, however, that these patients were in process of recovery and so the blood-sugar level would be declining with the return to normal metabolism (reference Table I).

*Response to Treatment*

As a result of studying the behaviour of the blood sugar following treatment, it was obvious that, where there was improvement in the condition of the patient, the blood-sugar level fell. This is well exemplified in the following patient (Case 1), who was admitted suffering from postpartum haemorrhage and who had been in shock for over 3 hours. The blood sugar before treatment was 238 mg. per cent and after receiving 3 pints of blood it had fallen to 183 mg. per cent; 8¾ hours after the initial blood-sugar reading the value was 131 mg. per cent. The pulse rate at these readings was 120, 102, and 80 per minute.

Despite the marked general improvement in their condition, in regard to colour, skin temperature, blood-pressure, mental reaction, and general well-being, it was noted that in some cases the pulse rate remained high and in these cases the fall in blood sugar was not so marked. Further study of these cases showed that the blood-sugar levels slowly declined in direct relationship with the fall in pulse rate. This is illustrated by Case 11.

## Summary

It is clear from the foregoing data that:

(1) Haemorrhagic shock occurring in various phases of pregnancy produces a hyperglycaemia, and

(2) that there is a definite relationship between the level of the blood sugar and the length of time which has elapsed between the onset of the shock and the taking of the sample. During the first 10 minutes little change occurs in the blood

sugar but thereafter there is a rapid increase and the longer the shock remains untreated the higher is the blood-sugar reading.

(3) In shock due to accidental haemorrhage the rate of response is slow, and the evidence suggests that this is due to an alteration in carbohydrate metabolism in toxaemia.

(4) The hyperglycaemia diminishes as the patient recovers from shock particularly with the aid of blood transfusion.

(5) There appears to be a direct relationship between the degree of hyperglycaemia and the amount of blood lost.

(6) If the patient suffers a second collapse, hyperglycaemia is repeated and the blood sugar returns to normal more slowly.

I wish to thank Professor R. A. Lennie, Professor D. F. Anderson, Dr. J. Hewitt, and their staffs, for the facilities granted; and the resident staff of the Glasgow Royal Maternity and Women's Hospital for their co-operation. To Dr. A. D. T. Govan I am much indebted for his constant advice and guidance in the preparation of this paper.

## References

Beecher, H. K. (1949): *Resuscitation and anesthesia for wounded men—the management of traumatic shock.* Thomas, Springfield, Illinois.

Clark, E. J., and Rossiter, R. J. (1944): *Quart. J. exp. Physiol.*, **32**, 269.

Engel, F. L., Winton, M. G., and Long, C. N. H. (1943): *J. exp. Med.*, **77**, 397.

Frank, H. A., Seligman, A. M., and Fine, J. (1946): *J. clin. Invest.*, **25**, 22.

Fraser, R., Albright, F., and Smith, P. H. (1941): *J. clin. Endocrinol.*, **1**, 297.

Herbert, F. K., and Bourne, M. C. (1930): *Biochem. J.*, **24**, 299.

Mukherjee, C. L., and Govan, A. D. T. (1950): *J. clin. Path.*, **3**, 274.

Nishi, M. (1909): *Arch. exp. Path. Pharmak.*, **61**, 186.

Robertson, J. D. (1935): *J. Physiol.*, **84**, 393.

Selye, H. (1950): *Brit. med. J.*, **1**, 1383.

Slocum, M. A., and Lightbody, H. D. (1931): *Amer. J. Physiol.*, **96**, 35.

Taylor, F. H. L., Levenson, S. M., and Adams, M. A. (1944): *New Engl. J. Med.*, **231**, 437.

Wiggers, C. J. (1950): *The physiology of shock.* Commonwealth Fund, New York.

# LATE EFFECTS OF EARLY AMBULATION IN OBSTETRICS

BY

H. B. ATLEE, I. A. PERLIN AND JEAN A. PEABODY

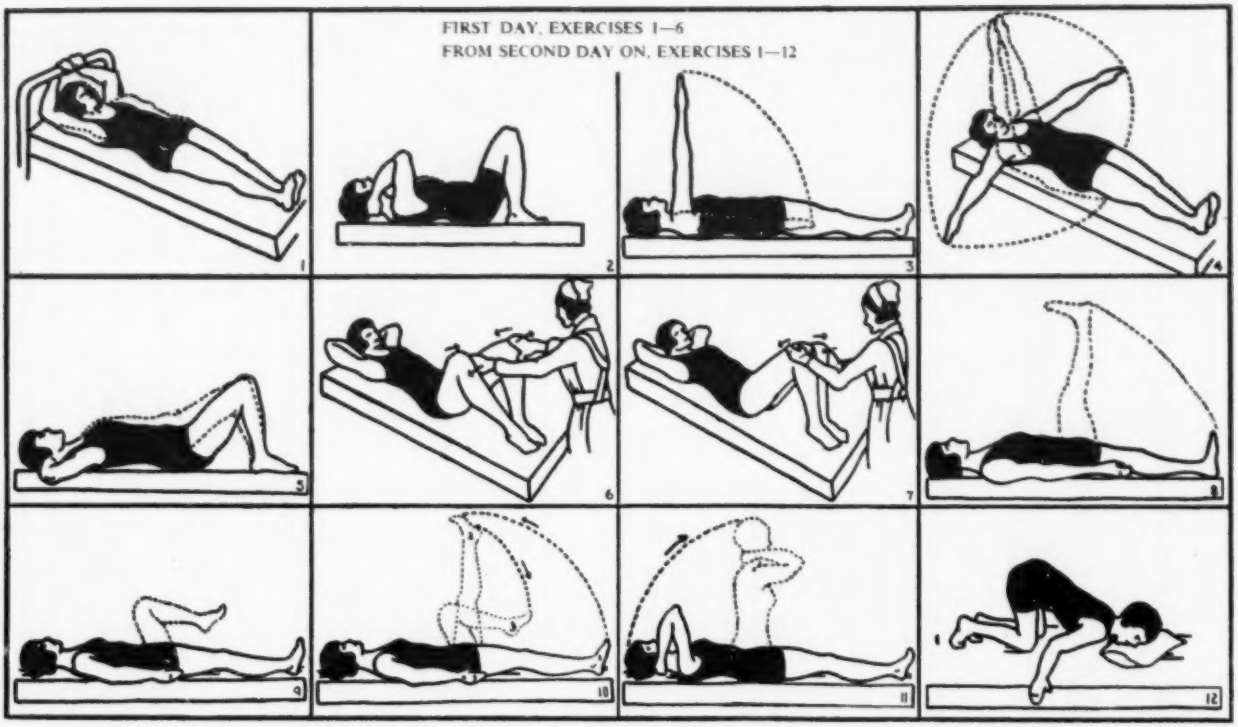
IN 1935 one of us (Atlee) reported on 500 cases delivered between 1928–34 who did exercises starting the day after delivery, and got out of bed and walked the day after that. The late Dr. J. B. DeLee criticized this active regime on three counts: it would increase the incidence of (1) subinvolution, (2) prolapse and (3) embolism.

Since none of these unhappy sequelae had developed up to that time, and since the women concerned were so overwhelmingly in favour of it (leaving hospital much more capable of looking after themselves—a not inconsiderable factor in an age of scarce domestic help), and since the study had already begun to cast some doubt on the textbook concepts of subinvolution and puerperal retroversion it was felt that it should be continued. While early ambulation has been given the stamp of approval by the latest edition of Greenhill-DeLee (1951), we believe that there is still considerable scepticism regarding it. As recently as 1948, Cornell and Mullen said: "Whether or not they (patients undergoing early ambulation) are going to have relaxed perineums for the gynaecologists to repair, prolapse and other things, it is difficult to say". This study is the first, so far as we have been able to ascertain, where an attempt has been made some years after early ambulation to bring to light late effects of it. Of the 1,118 women followed up all but 250 had done their early ambulating anywhere from 5 to 20 years previously, most of them from 7 to 20 years (see Table I). We feel that an effect that has not shown itself in 7 years can hardly be blamed on a puerperal regime.

The study embraces 2,157 women in 2,332 pregnancies, who undertook early ambulation between 1928–49, and an additional 300 women in 300 pregnancies studied since then to bring out certain additional facts not clearly established in the previous group. It includes an examination on the 10th day postpartum (8th day for the 1947–49, and 7th day for the recent 300 group—counting day of delivery as day no. 1), (2) an examination at the 6th week postpartum, (3) a questionnaire sent to those not coming for the 6th week examination, (4) a recent questionnaire sent to all cases delivered between 1928–49, (5) a search through the records of the gynaecological service to establish if any of those not answering (4) had been operated on there for any gynaecological condition, (6) recent examination of certain women answering (4) who complained of prolapse and other symptoms and (7) recent examination at the 7th day and 6th week of 300 women.

There are unavoidable hiatuses in our follow-up. Despite the strongest urging only one-third of our women came for the 6th week examination, only another third answered the 3-month questionnaire, and slightly more than half answered the final questionnaire. This was due to two factors, (1) during the war Halifax had a large shifting population, and (2) we were unable through press of work to carry on the study during the later war years. Nevertheless, the sum total of informaton obtained from all methods used gives, in so far as we can judge, a fair and reasonable picture of what happened to our women as a whole. We have no figures for comparing our late sequelae with those of women not undertaking early ambulation.

Before going further let us establish what we mean by early ambulation. On the day after delivery, the woman does the exercises shown on another page, and the day following that she gets out of bed and walks about. Each exercise is done 3 times every morning, requiring approximately 15 minutes for the lot. The exercises are done under the supervision of a nurse and in the large ward they were done in unison as she calls them out. No special value is claimed for any one of them. A great deal of stress is laid by some writers on the value of the




EXERCISE 1.—Grasp the rail at the head of the bed and draw yourself towards the head of the bed without lifting yourself from the bed. EXERCISE 2.—With knees bent and hands clasped behind head draw in your breath and at the same time draw your abdomen in as far as you can. Exhale, and at the same time try to keep your abdomen drawn in. EXERCISE 3.—With your elbows close in at your sides raise your arms straight into the air and lower them against the resistance of your own muscles. EXERCISE 4.—Lying flat on your back stretch your arms out wide and bring them slowly together above you against the resistance of your own muscles, keeping your arms stiff. Lower them slowly against the resistance of your own muscles. EXERCISE 5.—With knees bent and hands clasped behind head lift your body from the bed so that you are supporting yourself on your feet and shoulders. EXERCISE 6.—In same position as 5, spread your knees apart and then try to bring them together against the resistance of the nurse's hands. EXERCISE 7.—In the same position as 5, but with the knees close together, try to separate them against the resistance of the nurse's hands. EXERCISE 8.—With hands at sides and lying flat raise one stiff-held leg straight into the air, lower it and then raise and lower other leg. (If there is more than a first degree tear of perineum both legs should be raised at the same time.) EXERCISE 9.—In same position as 8 draw one leg up with bent knee as far as it will go and return to starting position. (If there is more than a first degree tear of perineum draw both legs at the same time.) EXERCISE 10.—In same position draw one stiff-held leg straight up, bend knee, and then press into abdomen with both hands. (If there is more than a first degree tear of perineum do this with both legs at same time.) EXERCISE 11.—With hands clasped behind head rise to a sitting position: then return slowly to starting position. EXERCISE 12.—In knee-chest position draw breath in as in Exercise 11 and expel breath the same way.

knee-chest position. We use it merely as another exercise. We have no evidence that it reduces the incidence of retroversion. If these exercises have any advantage over any other group that might have been chosen, it is that they tend more particularly to cause retraction of the lax abdominal muscles. All that we can truly say is that they tone up the whole muscular system, thus increasing the rapidity of the flow of blood through the involuting pelvic organs, and that (with the exception of No. 11) they are easy to do.

What activity does getting up entail? The 1st day up the patient gets out of bed on one side, walks around it to the other, and sits in a chair for 15 minutes, then walks around the bed again and gets into it. This is repeated the afternoon of the same day. If the patient is in a private room with a bath she is allowed to go to the toilet as soon as and whenever she wishes; if in the ward, or in a room too far removed from a toilet, she must endure the bedpan for the first day or two. This is the minimum of activity that has been undertaken by all the women in this study. We have found over the years that an increasing number of women will undertake more activity than the above and we do not restrict any woman who wishes to increase her mobility beyond the minimum just described. On the 2nd day up the activity is increased, and from that afternoon on all patients go to the bathroom when they need to. In the case of the ward patients this entails a walk of about 90 feet each way. Our ward supervisors estimate that about 75 per cent of patients do the minimum only on the 1st day, whereas the figure is reversed on the 2nd day and 75 per cent do more than the minimum. From the 2nd day up

TABLE I
*Number of Active Regime Puerperae Each Year*

| Year of delivery | NUMBER OF CASES: Total active puerperia | | 10th day exams | 6th week exams | 3rd month quest. | NUMBER OF WOMEN: doing last active puerperium | answered recent quest. or had recent exam. |
|---|---|---|---|---|---|---|---|
| 1928 | 6 | | — | — | 3 | 5 | — |
| 1929 | 23 | | — | — | 10 | 23 | 2 |
| 1930 | 18 | | — | — | 6 | 16 | — |
| 1931 | 32 | | — | — | 15 | 31 | 7 |
| 1932 | 52 | | — | — | 26 | 50 | 11 |
| 1933 | 81 | | — | — | 33 | 79 | 26 |
| 1934 | 62 | | — | — | 26 | 61 | 15 |
| | — | 274 | | | | | |
| 1935 | 50 | | 38 | 24 | 21 | 40 | 25 |
| 1936 | 117 | | 99 | 41 | 40 | 102 | 50 |
| 1937 | 120 | | 99 | 51 | 49 | 100 | 63 |
| 1938 | 147 | | 123 | 38 | 60 | 120 | 76 |
| 1939 | 207 | | 183 | 56 | 87 | 184 | 98 |
| 1940 | 247 | | 200 | 53 | 73 | 221 | 107 |
| 1941 | 270 | | 204 | 97 | 62 | 261 | 140 |
| 1942 | 201 | | 170 | 64 | 41 | 188 | 116 |
| 1943 | 157 | | 112 | 41 | 17 | 153 | 101 |
| | — | 1516 | | | | | |
| 1944 | 34 | | — | 34 | — | 29 | 11 |
| 1945 | 36 | | — | 36 | — | 32 | 20 |
| 1946 | — | | — | — | — | — | — |
| 1947 | 43 | | 26 | 10 | — | 42 | 16 |
| 1948 | 189 | | 120 | 53 | — | 188 | 95 |
| 1949 | 240 | | 157 | 99 | — | 232 | 139 |
| | — | 542 | | | | | |
| Total | 2332 | | 1531 | 697 | 569 | 2157 | 1118 |

onward most women are up and moving about or sitting in chairs talking and listening to the radio for most of the day.

Since 1947 we have allowed our women up on the day following delivery, and to go home from the 5th to 8th day. We have no evidence that this change has made any difference for better or worse, except that it represents an economic gain to the patient. Prior to 1936 patients with any degree of toxaemia, or any temperature above 100, did not follow the regime, but since that year only those with the severer types of toxaemia, or some unusual complication such as tuberculosis, heart failure, or pneumonia, remained inactive. We have described our regime in detail because it is our impression that early ambulation means considerably less than this to some writers. We do not consider it early ambulation if a woman is slid out of bed into a chair by a nurse, then lifted back in a few minutes. She must walk unsupported.

Table I shows the number of active puerperae in the 1928–49 group by years. It should be clear that the small numbers listed in the years 1944–47 do not represent all those who undertook early ambulation during those years, but only those whom we had time to study.

Tables II and III show the number of active puerperia undertaken by each woman and the puerperium in which she first undertook it.

The investigation was carried out in the following manner: (1) All the 10th day examinations in the 1928–43 group were done by one of us. (2) The 7th and 8th day examinations in the 1947–49 and the recent 300 cases were done by three staff members and residents trained by us. (3) All the 6th week examinations in the 1928–43 group were done by a single clinician. (4) All the 6th week examinations in the remaining groups were done by residents and three members of our department. (5) All the 3-months questionnaires asked the same questions over the entire period. (6) The final investigation was done by one of the authors under a Federal Health Grant (I.A.P.).

In carrying out the various examinations we all co-operated closely in order to achieve as nearly as possible uniformity of criteria. Of course, no two people estimate alike the size of the uterus by bimanual examination; nor will any one person judge it exactly the same day in and day out. Nor is it easy to make exact allowance for such distracting factors as thickness and resistance of the abdominal walls, amount of urine in the bladder (all women were sent to the toilet immediately before, but at the 6th week examination there might have been a time lapse in some of the cases). Moreover, definition of criteria presented its difficulties. What was a "large", a "medium", or a "small" uterus? An impression only. We decided that a "small" uterus was one that had involuted beyond what one of us from previous experience had judged to be the usual, or norm, for the particular day or week of the examination, which

TABLE II

*Number of Active Regime Puerperia Within Study Period*

| Active regime puerperia | No. in study | | No. answered recent quest. | |
|---|---|---|---|---|
| | Women | Cases | Women | Cases |
| 1 | 2013 | 2013 | 1014 | 1014 |
| 2 | 122 | 244 | 90 | 180 |
| 3 | 17 | 51 | 10 | 30 |
| 4 | 2 | 8 | 2 | 8 |
| 5 | 2 | 10 | 1 | 5 |
| 6 | 1 | 6 | 1 | 6 |
| Total | 2157 | 2332 | 1118 | 1243 |

TABLE III

*Order of Birth for First Active Puerperium*

| Order of birth | Women doing 1st active puerperium | | Percentage distribution of births N.S. 1944 |
|---|---|---|---|
| | No. | Percentage distribution | |
| 1st | 997 | 46.2 | 32.4 |
| 2nd | 393 | 18.2 | 22.9 |
| 3rd | 224 | 10.4 | 14.0 |
| 4th | 151 | 7.0 | 9.6 |
| 5th | 110 | 5.1 | 6.3 |
| 6th | 84 | 3.9 | 4.3 |
| 7th | 60 | 2.8 | 2.8 |
| 8th and over | 138 | 6.4 | 7.6 |
| Total | 2157 | 100.0 | 100.0 |

was called "medium"; and "large" would be one that was definitely bulky. One had the feeling that "small" and "medium" tended to merge into one another, so that a uterus designated as "small" one day might have been thought "medium" on another, and vice versa—whereas the "large" group had a greater constancy.

Pelvic floor damage was estimated by inspection of the perineum, with the labia held far apart and the woman bearing down as hard as she could; this bearing down was repeated with the fingers in the vagina to estimate uterine descent, and the mobility of the cervix and uterus, within the pelvis, was estimated by moving the latter with the fingers. While this procedure will not reveal every case of prolapse (some cases manifesting themselves only after the woman has been on her feet for some time) it does pick up the majority.

The colour of the lochia was estimated by inspecting the vulvar pads, and the usual text-book criteria concerning "rubra", "serosa", and "alba" were followed.

## Immediate Effects of Early Ambulation (10th day to 3rd month)

This study includes 1,531 women questioned and examined at the 7th–10th day; 697 examined and questioned at the 6th week; and 569 of those who did not come for (2) who answered the 3-month questionnaire. We made the attempt to determine (1) the size of the uterus, (2) the character and duration of the lochia, (3) the position of the uterus, (4) the presence of any pelvic floor damage or prolapse, (5) any other resultant pelvic abnormality, and (6) the attitude of the women towards the regime.

### *Size of the Uterus*

It is generally held that the uterus tends to be larger in a multipara than a primipara. Table IV shows our findings at the 10th day, and reveals a slight trend towards a small uterus in primiparae, and towards a large in multiparae, but by the 6th week (see Table V) this difference had disappeared, and there was actually a higher percentage of multiparae than primiparae with small uteri, the percentage with large being approximately the same.

Early activity does not seem to have increased the numbers with a large uterus at the 6th week. In women with an inactive puerperium Chassar Moir (1932) found 13 per cent of his uteri large at 5 weeks; our figure is 6.4 per cent large at 6 weeks. We checked the size of the uterus again at 6 weeks in 300 women recently undergoing an increased activity (see Table XIV) and obtained an even smaller percentage of large uteri

Table IV
*Size of Uterus at 10th Day*

| Size of uterus | No. of 10th day examinations | | | Percentage distribution | | |
|---|---|---|---|---|---|---|
| | Primiparae | Multiparae | Total | Primiparae | Multiparae | Total |
| Large | 92 | 194 | 286 | 16.7 | 19.8 | 18.7 |
| Medium | 147 | 334 | 481 | 26.7 | 34.0 | 31.4 |
| Small | 311 | 453 | 764 | 56.5 | 46.2 | 49.9 |
| Total | 550 | 981 | 1531 | 100.0 | 100.0 | 100.0 |

Table V
*Size of Uterus and Parity at 6th Week*

| Parity | Size of uterus | | | | | |
|---|---|---|---|---|---|---|
| | Large | | Medium | | Small | |
| | | per cent | | per cent | | per cent |
| Primiparae | 21 | (6.2) | 112 | (33) | 206 | (61) |
| Multiparae | 24 | (6.7) | 99 | (28) | 235 | (65) |
| Total | 45 | (6.4) | 211 | (30) | 441 | (63) |

(2.7 per cent) and an increased number of small uteri (73 per cent as against 63 per cent). Our evidence therefore is that the greater the puerperal activity the smaller the uterus will be at the 6th week. When those cases examined at the 10th day are followed to the 6th week, it is seen (Table VI) that involution did not always proceed in the direction of smallness. Generally speaking the uterus that is small at 10 days was also small at 6 weeks, but some uteri that were small and medium for 10 days were in a "larger" category at the 6th week, and most of the uteri that were large at the 10th day were small at the 6th week—only 3 out of 59 remaining in the "large" category. On the whole the tendency as the puerperium advances is towards mediocrity.

*Character of the Lochia*

While this was determined from day to day by inspection of the vulvar pads, we occasionally ran into a patient with a lochia serosa or alba from whose flabby uterus we could express a fair amount of lochia rubra on the 10th day, causing us to alter our estimation of the character of the lochia for that day. The results are shown in Tables VII to X. We have recently questioned 300 women at the 6th week who got up the day after delivery, as to the actual time after delivery at which all colour disappeared.

No notation was made in the case of the 697 patients of the original study as to the time of cessation of the lochia. We therefore checked this on a recent series of 300 cases, with the

TABLE VI
*Size of Uterus at Sixth Week According to Size at 10th day*

| Size of uterus at 10th day | Size of uterus at 6th week | | | |
|---|---|---|---|---|
| | Large | Medium | Small | Total |
| Large ... | 3 | 10 | 46 | 59 (14 per cent) |
| Medium ... | 4 | 38 | 72 | 114 (32 per cent) |
| Small ... | 4 | 38 | 133 | 175 (54 per cent) |
| Total ... | 11 (3 per cent) | 86 (24 per cent) | 251 (73 per cent) | 348 (100 per cent) |

TABLE VII
*Colour of Lochia at 10th Day*

| Colour of lochia | No. of 10th day examinations | | | Percentage distribution | | |
|---|---|---|---|---|---|---|
| | Primiparae | Multiparae | Total | Primiparae | Multiparae | Total |
| Rubra ... ... | 33 | 100 | 133 | 6.0 | 10.2 | 8.7 |
| Serosa ... ... | 286 | 497 | 783 | 52.0 | 50.7 | 51.1 |
| Alba ... ... | 220 | 357 | 577 | 40.0 | 36.4 | 37.7 |
| Absent ... ... | 11 | 27 | 38 | 2.0 | 2.8 | 2.5 |
| Total ... ... | 550 | 981 | 1531 | 100.0 | 100.0 | 100.0 |

TABLE VIII
*Amount of Lochia at 10th Day*

| Amount of lochia | No. of 10th day examinations | | | Percentage distribution | | |
|---|---|---|---|---|---|---|
| | Primiparae | Multiparae | Total | Primiparae | Multiparae | Total |
| Profuse ... ... | 115 | 144 | 259 | 20.9 | 14.7 | 16.9 |
| Moderate ... | 157 | 268 | 425 | 28.5 | 27.3 | 27.8 |
| Scant ... ... | 267 | 542 | 809 | 48.5 | 55.2 | 52.8 |
| Absent ... ... | 11 | 27 | 38 | 2.0 | 2.8 | 2.5 |
| Total ... ... | 550 | 981 | 1531 | 100.0 | 100.0 | 100.0 |

results shown in Table XI. Greenhill-DeLee (1951) states that the lochia ceases in from 3 to 6 weeks. This was true in approximately 90 per cent of our cases. Haultain and Irvine (1951) in 537 cases undergoing early ambulation found that in hospital cases it persisted over 28 days in only 13.3 per cent. Chassar Moir (1932), citing 250 cases not doing early ambulation, found that the lochia persisted over 28 days in 26 per cent of cases. The latter figure is closer to ours, although ours is higher than either: 47 per cent stopped flowing within 3 weeks, 42 per cent between 3 and 6 weeks, and 10 per cent still had some lochia at 6 weeks. As our active regime approximates closely that of Haultain and Irivine we find it difficult to explain the disparity in lochial disappearance.

We checked the date of termination of the lochia against both the size and position of the uterus, to determine if either of these tended to prolong it—as several authorities aver. There would appear to be a slight percentage trend towards prolongation of the lochia over 6 weeks in those cases with a uterus that was large either at the 7th day or the 6th week, although in actual number of cases only 2 out of 32 cases with such a persistent lochia were large. On the other hand approximately the same percentage of large as small ceased having a lochia by the end of 3 weeks (51.1 per cent against 50.4 per cent), and of those medium in size a considerably smaller percentage had a persistent lochia at 6 weeks than those small in size (2.8 per cent against 12.7 per cent). Such inconsistencies would suggest that it is hardly just to claim that size of uterus causes the lochia to be prolonged.

*What is Subinvolution?*

Before this study had been under way for many years we began to wonder about this entity. In the last edition of Williams (Eastman, 1950) it is thus described: "An arrest or retardation of the process of involution, by which the puerperal uterus is normally restored to its original proportions. The existence of subinvolution is manifested by a prolongation of the lochial discharge beyond the usual period, and sometimes by profuse haemorrhage, its cessation being followed by a persistent leucorrhea with pains in the back, a dragging down sensation, and a delayed return to perfect health. If this condition is not properly treated it may lead to permanent changes in the uterus and particularly its vessels which are sometimes associated with such persistent haemorrhage as eventually to necessitate removal of the organ. The diagnosis is established by bimanual examination, the uterus being found to be larger, softer and more succulent than it should be at a given time following delivery."

Greenhill-DeLee (1951) stigmatizes it as "a large, boggy uterus that bleeds on the slightest provocation", and adds that "if bleeding occurs during the recuperative period it is usually due to subinvolution". Henry and Goodwin (1951) quote McKerron as stating that "the clinical symptoms associated with uterine subinvolution are not so much the result of increased size of the organ or the pathological changes within it, as the result of the more generally incomplete involutional process which has involved the other pelvic tissues in addition, such as ligamentary and vascular structures, and the vagina. . . . From the clinical standpoint, a continued uniform enlargement of the uterus is the most outstanding evidence of subinvolution". A search through other standard textbooks and journal articles has added nothing to the above statements; in effect it appears that most obstetricians judge subinvolution by two criteria (1) size of the uterus and (2) character of the lochia, and feel that a large uterus and excessive lochial flow—constituting in their mind the entity subinvolution—play a part in the production of such future ill-effects as retroversion, menorrhagia, backache and other symptoms of chronic bad health. Let us say at the beginning that, either we did not have a true case of subinvolution in our series, or that if we did, our figures do not support this textbook definition. As the matter of size of the uterus and character of the lochia is pursued to the final questionnaire, it becomes more apparent that the large uterus is not a rogue uterus and that the character or duration of the lochia appears to determine no remote ill-effects in the absence of a retained fragment of placenta.

At the 10th day examination, as Tables IX

TABLE IX

*Colour and Amount of Lochia for Each Uterus Size at 10th day*

| Amount of lochia | Large | | | | | Medium | | | | | Small | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rubra | Serosa | Alba | Absent | Total | Rubra | Serosa | Alba | Absent | Total | Rubra | Serosa | Alba | Absent | Total |
| Profuse ... | 19 | 48 | 8 | — | 75 | 21 | 54 | 10 | — | 85 | 12 | 73 | 14 | — | 99 |
| Moderate ... | 23 | 55 | 10 | — | 88 | 19 | 98 | 28 | — | 145 | 16 | 123 | 53 | — | 192 |
| Scant ... | 4 | 64 | 50 | — | 118 | 8 | 110 | 120 | — | 238 | 11 | 158 | 284 | — | 453 |
| Absent ... | — | — | — | 5 | 5 | — | — | — | 13 | 13 | — | — | — | 20 | 20 |
| Total ... | 46 | 167 | 68 | 5 | 286 | 48 | 262 | 158 | 13 | 481 | 39 | 354 | 351 | 20 | 764 |

TABLE X

*Percentage Distribution of Colour and Amount of Lochia for Each Uterus Size at 10th Day*

| Amount of lochia | Large | | | | | Medium | | | | | Small | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rubra | Serosa | Alba | Absent | Total | Rubra | Serosa | Alba | Absent | Total | Rubra | Serosa | Alba | Absent | Total |
| Profuse ... | 6.6 | 16.8 | 2.8 | — | 26.2 | 4.4 | 11.2 | 2.1 | — | 17.7 | 1.6 | 9.6 | 1.8 | — | 13.0 |
| Moderate ... | 8.0 | 19.2 | 3.5 | — | 30.8 | 3.7 | 20.4 | 5.8 | — | 30.1 | 2.1 | 16.1 | 6.9 | — | 25.1 |
| Scant ... | 1.4 | 22.4 | 17.5 | — | 41.2 | 1.7 | 22.9 | 24.9 | — | 49.5 | 1.4 | 20.7 | 37.2 | — | 59.3 |
| Absent ... | — | — | — | 1.7 | 1.7 | — | — | — | 2.7 | 2.7 | — | — | — | 2.6 | 2.6 |
| Total ... | 16.1 | 58.4 | 23.8 | 1.7 | 100.0 | 10.0 | 54.5 | 32.8 | 2.7 | 100.0 | 5.1 | 46.4 | 45.9 | 2.6 | 100.0 |

TABLE XI

*Size of Uterus at 7th Day and 6 Weeks and Termination of Lochia*

| Size of uterus at 7th day and at 6th week | Total cases | Week lochia stopped | | | | | | | Total | Distribution of weeks, per cent | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 6+ | | 1, 2, 3 | 4, 5, 6 | 6+ |
| *Large* | 47 | 4 | 9 | 11 | 10 | 7 | – | 6 | 100.0 | 51.1 | 36.2 | 12.8 |
| Large ... ... | 5 | – | – | 3 | 1 | – | – | 1 | | 60.0 | | |
| Medium ... | 7 | 1 | 2 | 2 | 2 | – | – | – | | 71.4 | | |
| Small ... ... | 35 | 3 | 7 | 6 | 7 | 7 | – | 5 | | 45.7 | | |
| *Medium* | 128 | 10 | 22 | 22 | 24 | 26 | 10 | 14 | 100.0 | 42.2 | 46.9 | 10.9 |
| Large ... ... | 3 | – | 2 | – | – | – | – | 1 | | 66.7 | | |
| Medium ... | 34 | 2 | 6 | 10 | 4 | 8 | 3 | 1 | | 52.9 | | |
| Small ... ... | 91 | 8 | 14 | 12 | 20 | 18 | 7 | 12 | | 37.4 | | |
| *Small* | 125 | 9 | 26 | 28 | 26 | 17 | 7 | 12 | 100.0 | 50.4 | 40.0 | 9.6 |
| Large ... ... | — | – | – | – | – | – | – | – | | | | |
| Medium ... | 31 | 3 | 4 | 9 | 8 | 3 | 3 | 1 | | 51.6 | | |
| Small ... ... | 94 | 6 | 22 | 19 | 18 | 14 | 4 | 11 | | 50.0 | | |
| *Total* ... ... | 300 | 23 | 57 | 61 | 60 | 50 | 17 | 32 | 100.0 | 47.0 | 42.3 | 10.7 |
| Large ... | 8 | – | 2 | 3 | 1 | – | – | 2 | 100.0 | 62.5 | 12.5 | 25.0 |
| Medium ... | 72 | 6 | 12 | 21 | 14 | 11 | 6 | 2 | 100.0 | 54.2 | 43.0 | 2.8 |
| Small ... ... | 220 | 17 | 43 | 37 | 45 | 39 | 11 | 28 | 100.0 | 44.1 | 43.2 | 12.7 |

and X disclose, there is, true enough, a greater percentage tendency for the large rather than the medium or small uterus to have a profuse, red lochia, but both medium and small can have a profuse, red lochia. In actual numbers of cases (see Table IX) 19 large, 21 medium and 12 small uteri had such a lochia. On the other hand, while there was a greater tendency for the medium and still more for the small uteri to have a scant, alba lochia, nevertheless large uteri frequently had a scant white lochia—the actual figures being 50 large, 120 medium and 284 small.

Does size of the uterus play any part in producing those complaints that some women present during the puerperium? In a recent study of 300 women who were definitely asked at the 7th day if they had a complaint, the results are shown in Table XII:

The largest percentage of complainers came from the group with a medium-sized uterus although there were more complainers with a large than a small uterus (4.2 per cent to 1.6 per cent). At the 6th week examination we did not ask the 697 women of the 1928–49 group if they had a complaint and noted only 29 (4 per cent) who volunteered it. Out of a total of 41 women complaining at this time, only one had a large uterus. It would seem therefore that the size of the uterus, either at the 7th–10th day or 6th week, played little if any part in producing complaints such as those listed in Tables XIII and XIV.

Among those patients found to have any degree of uterine descent at the 6th week, there was a larger percentage of women with a large uterus than with either medium or small (4.4 per cent against 0.9 per cent and 1.1 per cent respectively)—see Table XV—but any significance that this might have disappears when Table XVI is studied. Of those who had a large uterus at the 10th day, 59 came for examination at the 6th week and none of these had uterine

TABLE XII

*Size of Uterus and Complaints at 7th Day*

| Size of uterus at 7th day | No. exam. | No. with complaint later | Complaint per cent |
|---|---|---|---|
| Large ... ... | 47 | 2 | 4.2 |
| Medium ... ... | 128 | 8 | 6.2 |
| Small ... ... | 125 | 2 | 1.6 |
| Total ... ... | 300 | 12 | 4.0 |

TABLE XIII

*Size and Position of Uterus at 6th Week According to Complaints at that Time (Complaints Volunteered)*

| | Anteverted | | | Retroverted | | | |
|---|---|---|---|---|---|---|---|
| | Large | Medium | Small | Large | Medium | Small | Total |
| Backache | – | – | 7 | – | 1 | – | 8 |
| Weakness, tiredness | – | – | 4 | – | 1 | 1 | 6 |
| Backache and abdominal pain | – | – | 1 | – | 1 | – | 2 |
| Pain in abdomen | – | – | 1 | – | – | – | 1 |
| Nervousness | – | – | 1 | – | – | – | 1 |
| Headaches | – | – | – | – | 1 | – | 1 |
| Menorrhagia | – | – | 1 | – | – | – | 1 |
| Discharge | – | – | 1 | – | 1 | – | 2 |
| Prolapse | – | – | 1 | – | – | – | 1 |
| Haemorrhoids | – | 1 | 3 | – | – | – | 4 |
| Breast abscess | – | – | 2 | – | – | – | 2 |
| Total | – | 1 | 22 | – | 5 | 1 | 29 (4 per cent) |

TABLE XIV

*Size of Uterus and Complaints Asked For*

| Size of uterus at 6th week | No. exam. | (Per cent) | No. with complaints attributable | Percentage with complaints attributable |
|---|---|---|---|---|
| Large | 8 | ( 2.7) | 1 | 12.5 |
| Medium | 72 | (24.0) | 4 | 5.6 |
| Small | 220 | (73.3) | 7 | 3.2 |
| | 300 | | 12 | 4.0 |

TABLE XV

*Size of Uterus and Uterine Descent at 10th Day and at 6th Week*

| | Size at 10th day | | | | Size at 6th day | | | |
|---|---|---|---|---|---|---|---|---|
| | Large | Medium | Small | Total | Large | Medium | Small | Total |
| Number examined | 286 | 481 | 764 | 1531 | 45 | 211 | 441 | 697 |
| Uterine descent | 4 | 6 | 4 | 14 | 2 | 2 | 5 | 9 |
| Uterine descent (per cent) | 1.4 | 1.2 | 0.5 | 0.9 | 4.4 | 0.9 | 1.1 | 1.3 |

TABLE XVI

*Uterine Descent at 10th Day and at 6th Week by size of Uterus at 10th Day*

| Size of uterus at 10th day | At 10th day | | | At 6th week | | |
|---|---|---|---|---|---|---|
| | No. examined | Uterine descent | Per cent uterine descent | No. examined | Uterine descent | Per cent uterine descent |
| Large | 286 | 4 | 1.4 | 59 | – | – |
| Medium | 481 | 6 | 1.2 | 114 | 1 | 0.9 |
| Small | 764 | 4 | 0.5 | 175 | 3 | 1.7 |
| Not examined | – | – | – | 349 | 5 | 1.4 |
| Total | 1531 | 14 | 0.9 | 697 | 9 | 1.3 |

descent; in fact, most of the cases of uterine descent occurred in women who had a small uterus at the 10th day.

If we are to charge the large uterus with any part in production of prolapse it seems that it should be the uterus that is large at the 10th day when the pelvic ligaments are at their laxest. We could produce no clear-cut evidence that the large uterus predisposes to, or is unusually associated with prolapse. Nor could we produce any such evidence that the uterus that is large or retroverted at the 10th day was conspicuously associated with those symptoms complained of at the 6th week or 3rd month (see Table XVII). The great majority of these complainers had a medium or small uterus at the 10th day.

Table XVIII shows the character of the lochia at the 10th day in these complainers. Here again, it would appear that the symptoms complained of arose in women with every type of lochia except profuse alba. We feel that our findings do not support therefore the italicized (by us) part of the following statement in Williams's textbook: "The existence of subinvolution is manifested by a prolongation of the lochial discharge beyond the usual period, and sometimes by profuse haemorrhage, its cessation being followed by *persistent leucorrhea with pains in the back, a dragging-down sensation, and a delayed return to perfect health.*"

We have been struck, not only in this study but in investigating patients not included in it, by the difficulty of discovering anything in the pelvic organs or the state of pelvic ligamenture either at the 10th day or subsequently, to account for the backache so frequently complained of by puerperal women in the early months following labour.

In most instances it is located in the muscular, rather than the sacral region of the back; and the ready way in which it sometimes disappears when the woman is urged to adopt a better posture, or to exercise her back muscles, and to lift her heavy baby with her muscles rather than her ligaments, leads us to suspect that in a fair number of cases the cause is orthopaedic.

Many of these complainers have such obviously neurotic stigmata as tiredness, weakness, dizziness and nervousness (either alone or in combination), as to suggest that they represent a failure to make a full emotional recovery from childbirth. We use the word "suggest" because we do not know; these are only impressions for which we have no proof. We do feel, however, that our study seems to show that the cause of the symptoms complained of by women who have recently had children lies frequently in no clearly demonstrable pelvic lesion, and that such complaints arise irrespective of the size or position of the uterus, or of the amount or character or duration of the lochia.

Why does one woman have a profuse red lochia on a certain day and another a scant alba? Why does the coloured lochia disappear in one

TABLE XVII

*Specified Complaints at 6th week or 3rd Month According to Size and Position of Uterus at 10th Day*

| Complaints | Retroverted | | | Anteverted | | | Not examined | Total |
|---|---|---|---|---|---|---|---|---|
| | Large | Medium | Small | Large | Medium | Small | | |
| Backache | – | 1 | 1 | 3 | 9 | 22 | 2 | 38 |
| Pain in abdomen | – | 1 | – | 6 | 4 | 9 | – | 20 |
| Pain in abdomen and back | – | – | – | 3 | 1 | 2 | – | 6 |
| Tiredness, weakness, dizziness | – | – | – | 1 | 5 | 14 | 2 | 22 |
| Discharge | – | – | – | 2 | 3 | 3 | 1 | 9 |
| Discharge and backache | – | – | – | 1 | – | – | – | 1 |
| Menorrhagia | – | – | – | 1 | 3 | 1 | – | 5 |
| Nervousness | – | – | – | – | 3 | 2 | – | 5 |
| Headaches | – | – | – | – | – | 3 | 1 | 4 |
| Falling of womb | – | – | – | – | 1 | – | 1 | 2 |
| Pain in vagina | – | – | – | – | – | 1 | – | 1 |
| Haemorrhoids | – | – | – | 1 | 1 | 7 | – | 9 |
| Breast abscess | – | – | – | – | – | 2 | – | 2 |
| Total | – | 2 | 1 | 18 | 30 | 66 | 7 | 124 |

TABLE XVIII

*Specified Complaints at 6th Week or 3rd Month According to Character of Lochia at 10th Day*

| Complaints | Profuse | | | Moderate | | | Scanty | | | ABS | Not examined | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rubra | Serosa | Alba | Rubra | Serosa | Alba | Rubra | Serosa | Alba | | | |
| Backache ... ... ... ... ... | 4 | 6 | – | 1 | 8 | 1 | – | 7 | 8 | 1 | 2 | 38 |
| Pain in abdomen ... ... ... | – | 4 | – | – | 4 | 2 | – | 3 | 7 | – | – | 20 |
| Pain in abdomen and back ... | – | 1 | – | 1 | 1 | – | 1 | 2 | – | – | – | 6 |
| Tiredness, weakness, dizziness | 1 | 6 | – | 1 | 4 | – | – | 3 | 4 | 1 | 2 | 22 |
| Discharge ... ... ... ... ... | – | 2 | – | – | 1 | 1 | – | 3 | 1 | – | 1 | 9 |
| Discharge and backache ... ... | – | 1 | – | – | – | – | – | – | – | – | – | 1 |
| Menorrhagia ... ... ... ... | 1 | 1 | – | 1 | 1 | – | – | – | 1 | – | – | 5 |
| Nervousness ... ... ... ... | – | – | – | – | – | 2 | – | 2 | 1 | – | – | 5 |
| Headaches ... ... ... ... | – | 1 | – | – | 1 | – | – | – | 1 | – | 1 | 4 |
| Falling of womb ... ... ... | 1 | – | – | – | – | – | – | – | – | – | 1 | 2 |
| Pain in vagina ... ... ... ... | – | – | – | – | 1 | – | – | – | – | – | – | 1 |
| Haemorrhoids ... ... ... ... | 1 | 1 | – | – | – | – | – | 5 | 2 | – | – | 9 |
| Breast abscess ... ... ... ... | – | – | – | – | – | – | – | 1 | 1 | – | – | 2 |
| Total ... ... ... ... ... ... | 8 | 23 | – | 4 | 21 | 6 | 1 | 26 | 26 | 2 | 7 | 124 |
| Percentage ... ... ... ... | 6.4 | 18.5 | – | 3.4 | 17 | 4.8 | 0.8 | 21 | 21 | 1.6 | 5.6 | 100 |

woman, never to return, as early as the second week, yet persist in another on and off for upwards of 6 weeks? Certainly, our figures would not support any contention that the size or even the position (as will presently be shown) of the uterus gives a consistent answer. Of the large uteri only 26.6 per cent had a profuse lochia and only 6.6 per cent a profuse red lochia. So far as we can determine there were only 2 cases in which placental tissue was retained, and in both it was found lying free in the cervix and from there removed on the 10th day. Four curettages had to be done in the 1,118 women who answered our recent questionnaire, but in no case was this done for placental fragments retained following delivery, and in all 4 cases it was done some years following delivery. Nor did infection seem to play any part in altering the lochia—at least such infection as these patients had. Many of them ran a low-grade temperature for one or more days, but we could not see that this had any effect on the lochia. We are therefore still left wondering why this great variation in the character of the lochia exists: could an endocrine factor be responsible? We are also left asking ourselves if there is such an entity as subinvolution, or if there is, if it has any clinical significance.

*Puerperal Retroversion*:

Of the 1,531 women examined at the 10th day 57, or 3.7 per cent, were retroverted; of 300 women recently examined on the 7th day, 16, or 5.3 per cent, were retroverted. At the 6th week we found 110, or 15.8 per cent, of the 697 women who were examined on the 10th day to have a retroverted uterus, and 80, or 25.6 per cent of the 300 cases examined on the 7th day (see Tables XIX and XX). The figures reported by different writers on the incidence of retroversion at this time are even more varied than our two sets. Moses (1939) reported 35 per cent, Peckham (1934) 18 per cent, and Haultain and Irvine (1951), following an active regime similar to ours, only 6.7 per cent in 537 cases. Lynch (1922), examining cases regularly up to a year,

TABLE XIX
*Position of Uterus at 6th Week According to Position at 10th Day*

| Position of uterus at 10th day | Number examined at 10th day | Position of uterus at 6th week | | |
|---|---|---|---|---|
| | | Retroverted | Anteverted | Number examined at 6th week |
| Retroverted ... ... | 57 | 5 | 3 | 8 |
| Anteverted ... ... ... | 1474 | 59 | 281 | 340 |
| Not examined ... ... | — | 46 | 303 | 340 |
| Total ... ... ... ... | 1531 | 100 | 587 | 697 |

TABLE XX
*Position of Uterus 7th Day and 6th Week and Termination of Lochia*

| Position of uterus at 7th day and 6th week | Total cases | Week lochia stopped | | | | | | | Percentage distribution of weeks | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 6+ | Total | 1, 2, 3, | 4, 5, 6 | 6+ |
| RETROVERSION | 16 | 4 | 5 | 2 | 2 | 1 | 1 | 1 | 100.0 | 68.8 | 25.0 | 6.2 |
| Retroversion ... | 8 | 1 | 4 | 1 | – | – | 1 | 1 | | 75.0 | | |
| Anteversion ... | 8 | 3 | 1 | 1 | 2 | 1 | – | – | | 62.5 | | |
| ANTEVERSION | 284 | 19 | 52 | 59 | 58 | 49 | 16 | 31 | 100.0 | 45.8 | 43.3 | 10.9 |
| Retroversion ... | 72 | 2 | 13 | 19 | 13 | 10 | 3 | 12 | | 47.2 | | |
| Anteversion ... | 212 | 17 | 39 | 40 | 45 | 39 | 13 | 19 | | 45.3 | | |
| TOTAL | 300 | 23 | 57 | 61 | 60 | 50 | 17 | 32 | 100.0 | 47.0 | 42.3 | 10.7 |
| Retroversion ... | 80 | 3 | 17 | 20 | 13 | 10 | 4 | 13 | 100.0 | 50.0 | 33.8 | 16.2 |
| Anteversion ... | 220 | 20 | 40 | 41 | 47 | 40 | 13 | 19 | 100.0 | 45.9 | 45.4 | 8.6 |

found that as many as 41 per cent were retroverted at one time or another during that period. Peckham (1934) found that, whereas 18 per cent were retroverted at 6 weeks, 16.8 per cent were in that position at the end of the year. The figures for others reporting seem to lie within the above quoted limits.

The significant thing that comes out of the studies of those who follow their retroversions for 6 weeks or more postpartum is that any position of the uterus is not necessarily permanent. An organ that is retroverted at one examination may be anteverted at another and vice versa. Of our 57 women with retroversion at the 7th day in the 697 group we were only able to examine 8 at the 6th week, but 3 had become anteverted (see Table XIX), and, of the 16 cases of the recent 300 group retroverted at the 7th day, no fewer than 8 were anteverted at 6 weeks (see table XX). We feel that this point is worthy of emphasis for the reason that most textbooks, while perhaps not directly stating so, leave it to be inferred that retroversion is a permanent position once it occurs. This inference is further strengthened by the obsession of some men with the necessity of immediately exhibiting such supposedly corrective measures as the knee-chest position and replacement-pessary treatment. We have found this change of position to occur also in nulliparae.

Findley (933) holds that "a retroversion existing prior to pregnancy, almost invariably becomes retroverted postpartum". This is a difficult statement to prove, since we so seldom get a chance to examine our patients before they become pregnant. Whether or not it is true, we doubt that it is true in all cases—otherwise why would a uterus that is retroverted at one time become anteverted at another, and vice versa? Let us restate the three common causes of puerperal retroversion given in the textbooks and see how they stand up under the scrutiny of the 6th week examination.

According to the textbooks retroversion of the uterus is produced puerperally in the following ways: (1) injuries of childbirth cause damage to or stretching of the various uterine supports, (2) a large and heavy uterus tends to fall over backwards while the woman is lying on her back in bed, and (3) over-distension of the bladder tends to push the puerperal uterus over on its back. The following statement by Hendry and Goodwin (1951) covers most of the causative grounds generally held:

"The commonest variety of acquired retroversion occurs after parturition as a result of relaxation of the uterine supports. . . . Permanent laxity (of the uterine supports) may develop as a result of prolonged labour, unwise instrumentation, puerperal infection, subinvolution, too early a return to the upright position, or too prolonged an employment of the dorsal position, the effect of which is to make the heavy uterus gravitate backward towards the sacrum. Habitual overdistension of the bladder is a frequent predisposing cause, as are intercurrent diseases, pelvic lacerations and long lactation periods with resultant genital atrophy. Williams and others believe that retroversion is due not so much to relaxation of the uterine ligaments as to undue stretching of the tissues at the base of the broad ligament, which are spread apart by the act of labour and which usually have not retracted when the woman begins to move about. A large uterus is therefore not properly supported, and displacement inevitably occurs, although always after the second week; prior to that time displacement cannot occur since the uterus is too large to be contained in the true pelvis."

The above boils down to the three factors previously mentioned: (1) damage to the uterine supports, (2) a large uterus whose weight carries it over backward with the woman lying on her back, and (3) overdistension of the bladder pushing the uterus over backward.

(1) *Damage to Uterine Supports*

Table XXI shows the incidence of damage to the pelvic floor and the uterine supports at the 10th day. Since the entity "relaxed perineum" in that table does not include pelvic floor damage, we have subtracted it from the total, which leaves 132 cases which showed some evidence of laxity of the uterine supports. Table XXII shows the incidence of retroversion in this group. While there is a slight trend towards increase of retroversion in association with pelvic floor damage, it is very slight. Almost

TABLE XXI
*Pelvic Floor Damage 10th Day*

| Condition of pelvic floor | Primiparae | Multiparae | Total |
|---|---|---|---|
| Slight rectocele ... ... ... ... ... ... | – | 13 | 13 |
| Slight cystocele ... ... ... ... ... | – | 4 | 4 |
| Slight cystocele and rectocele ... ... ... | – | 2 | 2 |
| Cystocele plus ... ... ... ... ... ... | – | 47 | 47 |
| Rectocele plus ... ... ... ... ... ... | 1 | 22 | 23 |
| Cystocele plus and rectocele plus ... ... ... | – | 16 | 16 |
| Cystocele plus and rectocele 2-plus ... ... | – | 2 | 2 |
| Cystocele 2-plus and rectocele plus ... ... | – | 4 | 4 |
| Cystocele 2-plus ... ... ... ... ... | – | 5 | 5 |
| Cystocele 2-plus and rectocele 2-plus ... ... | – | 2 | 2 |
| Uterine descent plus ... ... ... ... ... | – | 11 | 11 |
| Uterine descent 2-plus ... ... ... ... ... | – | 3 | 3 |
| Relaxed perineum ... ... ... ... ... | 37 | 350 | 387 |
| Total ... ... ... ... ... ... ... ... | 38 | 481 | 519 |
| Total pelvic floor damage only ... ... ... | 1 | 131 | 132 |

TABLE XXII
*Retroversion and Pelvic Floor Damage*

| | At 10th day | | | Pelvic floor damage per cent | At 6th week | | | Pelvic floor damage per cent |
|---|---|---|---|---|---|---|---|---|
| | Pelvic floor damage | No pelvic floor damage | Total | | Pelvic floor damage | No pelvic floor damage | Total | |
| Retroversion | 7 | 50 | 57 | 12.3 | 14 | 96 | 110 | 12.7 |
| Anteversion | 125 | 1349 | 1474 | 8.5 | 52 | 535 | 587 | 8.8 |
| Total | 132 | 1399 | 1531 | 8.6 | 66 | 631 | 697 | 9.5 |
| Retroversion (per cent) | 5.3 | 3.6 | 3.7 | | 21.2 | 15.2 | 15.8 | |

as great a percentage of cases showing no pelvic damage had a retroverted uterus—in actual numbers 125 of the 132 cases of pelvic floor damage had an anteverted uterus—which would suggest that some other factor than laxity of the uterine supports causes retroversion at the 10th day.

Table XXII shows the incidence of retroversion in those cases that had pelvic floor damage at both the 10th day and the 6th week. While there is a slightly greater percentage of retroversion in cases with pelvic floor damage (21.2 per cent as against 15.2 per cent), no fewer than 96, or 87 per cent of the 110 retroversions present at the 6th week occurred in women with no apparent pelvic damage. While we cannot therefore say that pelvic floor damage does not cause retroversion, we can say that it must represent a small factor in its production, and that some other factor than damage is responsible for most of the retroversions we found.

(2) *Size of the Uterus and Retroversion*

Tables XXIII and XXV show the incidence of retroversion in the different sized uteri at the 10th day and at the 7th. In Table XXIII the percentage of retroverted uteri is greater (5.2 per cent to 2.5 per cent) in the large than in the small, but in Table XXV the percentage is less in the large than in the small (2.1 per cent to 3.3 per cent). In actual numbers, if the figures of the two tables be combined, 33 medium and 20 small but only 16 large uteri were found retroverted at this time. It would seem therefore that there must be some other factor besides size that caused retroversion in the majority of those

found retroverted. Another phenomenon we find difficult to reconcile with size as cause of retroversion is that most puerperal retroversions occur between the end of the 1st week and the 6th week at a time when the uterus has become relatively small.

But whereas at the 10th day there was a slightly greater tendency for the large uterus to be retroverted when only 3.7 per cent of all uteri were in that position, at the 6th week, when 15.8 per cent were retroverted, a much higher percentage of small and medium (12.7 per cent and 23.7 per cent) than large (8.9 per cent) were found retroverted (Table XXIII). When actual numbers of cases are taken into consideration, it would seem that when 42 medium and small as against 15 large uteri are found retroverted at the 10th day, and 106 medium and small as against 4 are found retroverted at the 6th week, some other factor than size is responsible for this position in the great majority of cases.

(3) *Overdistension of the Bladder*

Catheterization had to be done very seldom in our patients. Once they were out of bed their ability to pass urine appeared quite normal. It certainly was normal at the time retroversion was most likely to occur, that is, after the first few days; and it was certainly normal in that period between the end of the 1st and the 6th week, when most of the retroversions occurred.

We would like to refer back to a previously quoted statement. "A large uterus is therefore not properly supported (when there is laxity of the uterine supports), and displacement *inevitably* occurs: although *always* after the 2nd week; prior to that time displacement *cannot* occur since the uterus is too large to be contained in the true pelvis." Our findings do not support the three words in italics in this statement (our italics). Displacement did not inevitably occur in those patients with a large uterus and laxity of the pelvic ligaments. Displacement did not always occur after the 2nd week. Table XXV shows that out of 300 cases examined at the 7th day, 16 retroversions had taken place—so displacement *can* occur prior to 2 weeks.

*Uterine Drainage and Retroversion*

Many textbooks state that the retroverted uterus drains less efficiently than the anteverted,

TABLE XXIII

*Size of Uterus and Retroversion at 10th Day and at 6th Week*

| | Size at 10th day | | | | Size at 6th week | | | |
|---|---|---|---|---|---|---|---|---|
| | Large | Medium | Small | Total | Large | Medium | Small | Total |
| Number examined ... ... ... ... | 286 | 481 | 764 | 1531 | 45 | 211 | 441 | 697 |
| Number retroversions ... ... ... | 15 | 23 | 19 | 57 | 4 | 50 | 56 | 110 |
| Retroversion (per cent) ... ... | 5.2 | 4.8 | 2.5 | 3.7 | 8.9 | 23.7 | 12.7 | 15.8 |

TABLE XXIV

*Character of Lochia and Retroversion at 10th Day*

| Amount of lochia | Rubra | | | Serosa | | | Alba | | | Absent | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. exam. | No. retrov. | Per cent | No. exam. | No. retrov. | Per cent | No. exam. | No. retrov. | Per cent | No. exam. | No. retrov. | Per cent | No. exam. | No. retrov. | Per cent |
| Profuse ... | 52 | 2 | 3.8 | 175 | 2 | 1.1 | 32 | 1 | 31 | – | – | – | 259 | 5 | 1.9 |
| Moderate ... | 58 | 2 | 3.4 | 276 | 7 | 2.5 | 91 | 5 | 5.5 | – | – | – | 425 | 14 | 3.3 |
| Scanty ... | 22 | 2 | 8.3 | 332 | 12 | 3.6 | 454 | 21 | 4.6 | – | – | – | 809 | 35 | 4.3 |
| Absent ... | – | – | – | – | – | – | – | – | – | 38 | 3 | 7.3 | 38 | 3 | 7.3 |
| Total .. | 133 | 6 | 4.5 | 783 | 21 | 2.7 | 577 | 27 | 4.7 | 38 | 3 | 7.3 | 1531 | 57 | 3.7 |

and that retroversion tends to prolong and increase the amount of lochial flow. A study of Tables XXIV, XXV and XXVI shows that this did not seem to be true with regard to our cases. Table XXIV reveals that the percentage of those with a profuse lochia is actually lower than those with a scant lochia in the retroverted cases (1.9 per cent to 4.3 per cent). The same is true of the matter of colour or colour and profuseness combined. Tables XXV and XXVI show that the percentage of those whose lochia lasted more than 6 weeks was slightly less in the retroverted than the anteverted uteri—certainly no greater; it will be seen also that 68 per cent of retroverted uteri ceased having a lochia under 3 weeks, as against 45.8 per cent of anteverted. Therefore, neither at the 10th day nor at the 6th week could we find any clear evidence that retroversion interferes with uterine drainage, or prolongs the lochial flow. In this connection Chassar Moir (1932) found that " the average duration of the coloured lochia in cases of . . . retroversion was not greater than the average of the total number of cases ". In actual numbers only 13 of our 32 cases with prolonged lochia (over 6 weeks) were retroverted. It would seem therefore that in the other 19 cases some other factor than retroversion must have been responsible for prolongation of the flow beyond 6 weeks. Could not this same factor have been responsible in all?

*Retroversion and Complaints*

It is generally felt that such complaints as backache, pelvic pain, etc., and excessive duration of the lochia, are caused by retroversion. In the 300 cases specially investigated for this purpose, we could find no evidence of this.

All the complaints at the 7th day in this group were from women with an anteverted uterus, and at the 6th week the percentage of complainers is roughly the same in both positions of the uterus (see Tables XXVII and XXVIII).

In the group that got up on the 10th day and volunteered complaints (see Table XIII) at the 6th week investigation only 6 of the 29 complainers had a retroverted uterus, or about 20 per cent. But as 20 per cent appears to be approximately the average incidence of retroversions in all puerperal women, the number of retroversions among the complainers is about what could have been expected. In other words, the woman with the retroversion is no more likely to have complaints than her sister with anteversion. It is our impression from reading the textbooks that a contrary view is the one commonly held. Consider the symptom backache, so frequently blamed on the retroverted uterus. Table XIII shows that, while 7 women with an anteverted uterus complained of it, only 1 with a retroverted uterus did so. Admittedly, the figures are too small to be conclusive, never-

TABLE XXV

*Size and Position of Uterus 7th Day and Duration Lochia*

| Size and position of uterus at 7th day | Total cases | Week lochia stopped | | | | | | | Percentage distribution of weeks | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 6+ | Total | 1, 2, 3 | 4, 5, 6 | 6+ |
| LARGE | 47 | 4 | 9 | 11 | 10 | 7 | – | 6 | 100.0 | 51.1 | 36.2 | 12.8 |
| Retroversion ... | 1 | 1 | – | – | – | – | – | – | | 100.0 | | |
| Anteversion ... | 46 | 3 | 9 | 11 | 10 | 7 | – | 6 | | 50.0 | | |
| MEDIUM | 128 | 10 | 22 | 22 | 24 | 26 | 10 | 14 | 100.0 | 42.2 | 46.9 | 10.9 |
| Retroversion ... | 11 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | | 54.5 | | |
| Anteversion ... | 117 | 8 | 20 | 20 | 22 | 25 | 9 | 13 | | 41.0 | | |
| SMALL | 125 | 9 | 26 | 28 | 26 | 17 | 7 | 12 | 100.0 | 50.4 | 40.0 | 9.6 |
| Retroversion ... | 4 | 1 | 3 | – | – | – | – | – | | 100.0 | | |
| Anteversion ... | 121 | 8 | 23 | 28 | 26 | 17 | 7 | 12 | | 48.8 | | |
| TOTAL | 300 | 23 | 57 | 61 | 60 | 50 | 17 | 32 | 100.0 | 47.0 | 42.3 | 10.7 |
| Retroversion ... | 16 | 4 | 5 | 2 | 2 | 1 | 1 | 1 | 100.0 | 68.8 | 25.0 | 6.2 |
| Anteversion ... | 284 | 19 | 52 | 59 | 58 | 49 | 16 | 31 | 100.0 | 45.8 | 43.3 | 10.9 |

TABLE XXVI

*Size and Position of Uterus at 6th Week and Duration of Lochia*

| Size and position of uterus at at 6th week | Total cases | Week lochia stopped | | | | | | | Percentage distribution of weeks | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 6+ | Total | 1, 2, 3 | 4, 5, 6 | 6+ |
| LARGE | 8 | – | 2 | 3 | 1 | – | – | 2 | 100.0 | 62.5 | 12.5 | 25.0 |
| Retroversion ... | 5 | – | 1 | 3 | – | – | – | 1 | | 80.0 | | |
| Anteversion ... | 3 | – | 1 | – | 1 | – | – | 1 | | 33.3 | | |
| MEDIUM | 72 | 6 | 12 | 21 | 14 | 11 | 6 | 2 | 100.0 | 54.2 | 43.0 | 2.8 |
| Retroversion ... | 19 | – | 4 | 5 | 4 | 3 | 2 | 1 | | | | |
| Anteversion ... | 53 | 6 | 8 | 16 | 10 | 8 | 4 | 1 | | | | |
| SMALL | 220 | 17 | 43 | 37 | 45 | 39 | 11 | 28 | 100.0 | 44.1 | 43.2 | 12.7 |
| Retroversion ... | 56 | 3 | 12 | 12 | 9 | 7 | 2 | 11 | | | | |
| Anteversion ... | 164 | 14 | 31 | 25 | 36 | 32 | 9 | 17 | | | | |
| TOTAL | 300 | 23 | 57 | 61 | 60 | 50 | 17 | 32 | 100.0 | 47.0 | 42.3 | 10.7 |
| Retroversion ... | 80 | 3 | 17 | 20 | 13 | 10 | 4 | 13 | 100.0 | 50.0 | 33.8 | 16.2 |
| Anteversion ... | 220 | 20 | 40 | 41 | 47 | 40 | 13 | 19 | 100.0 | 45.0 | 45.4 | 8.6 |

TABLE XXVII

*7th Day Retroversion and Complaints*

| Position of uterus at 7th day | No. examined | No. with complaints later | Per cent complaints |
|---|---|---|---|
| Retroversion | 16 | — | — |
| Anteversion | 284 | 12 | 4.2 |
| Total | 300 | 12 | 4.2 |

TABLE XXVIII

*6th Week Retroversion and Complaints*

| Position of uterus at 6th week | No. examined | No. with complaints attrib. | Per cent with complaints attrib. |
|---|---|---|---|
| Retroversion | 80 | 3 | 3.8 |
| Anteversion | 220 | 9 | 4.1 |
| Total | 300 | 12 | 4.0 |

theless they do raise the ironic question: Since backache occurred 7 times more frequently in anteversion than in retroversion, was not anteversion the cause of the backache?

*What should be done with the puerperally retroverted uterus?*

There is some difference of opinion on this point. Fischmann (1950) holds that " every new mother be examined from three to five weeks postpartum, and, if any disorder such as a retroverted uterus be discovered, measures for the correction of that condition be instituted at once ". Mayes (1950) feels that " insertion of a pessary is a debatable point. One's own experience has been disappointing ". Moses (1939) states: " The number of patients developing retroversion at the 6th week was the same in 210 women who did the knee-chest position as in the 210 who did not—35 per cent retroverted at 6 weeks ".

Greenhill-DeLee (1951) states the case for the in-betweeners as follows: " If retroversion is found and the uterus is enlarged and somewhat softened, the patient should be instructed to practise the knee-chest position. If the uterus is not enlarged and softened and the patient has no symptoms, these exercises are not essential to her well-being. In cases of retroflexion and subinvolution, if the uterus remains unchanged despite the knee-chest position and various exercises, it should be anteflexed and a hard rubber pessary inserted into the vagina and left there for two months. If the retroversion persists after removal of the pessary but produces no symptoms, no further treatment is given. However, if symptoms are present when the uterus remains retroverted and these symptoms are not present when the uterus is elevated with a pessary, an operation for suspension of the

uterus is justified". Since Williams, another of our leading textbooks, takes approximately the same stand, we can assume that this probably represents the majority practice on this continent.

Our own practice throughout this entire investigation was to leave the uterine fundus where it lay. True enough, we utilize the knee-chest position as one of our exercises—not because we feel it cures retroversion, but because it gives variety to our exercises. It is therefore instructive to see what happens ultimately when such a hands off procedure is followed. The results will appear under the final questionnaire.

*Did Early Ambulation increase the incidence of Prolapse?*

We found very little difference between the incidence of relaxed perineum at the 10th day and 6th week (25.3 per cent to 20 per cent). Of those found relaxed on the 10th day 28 were not relaxed at the 6th week and of those found relaxed at the 6th week 29 had not been so found at the 10th day.

Table XXIX reveals the picture of all pelvic floor damage over and above simple relaxation of the perineum at the 6th week. Of these cases there were 9 with definite uterine descent. The only recent figures we have found for comparison with these at a similar time after delivery are those of Salmond and Dearnley (1935) who examined at 2-months postpartum and found 25 per cent had anatomical results, of which about half had symptoms; and Nelson and Abramson (1941), who found about 10 per cent with moderately relaxed perinei and/or cystocele and 1 per cent with prolapse at their 6th week examination. The women in these two surveys were not on an active regime, Nelson and Abramson getting their patients out of bed for the first time on the 8th to 10th day. Our similar figures would be 9.5 per cent with any degree of prolapse, and 20 per cent with any degree of perineal relaxation. Although differently tabulated, the results would appear to be about the same. We have therefore no evidence at the 6th week that early ambulation increases the incidence of prolapse.

*Does Activity Tend to Break Down a Sutured Perineum?*

We wondered at first if the activity, and especially the exercises, might pull sufficiently on the perineal sutures as to cause breakdown of the episiotomies. In the early years we asked those with deep episiotomies to do the exercises with their legs held together. But as time went on and we gained confidence, we made no difference in the type of activity no matter how deep the perineal wound. We have noticed no increase in breakdown—indeed, it is our impression that the improved vaginal drainage, due to activity and the upright position, actually favours the healing of the perineum. This is also the impression of our nurses. In any case, there was no single case of breakdown of a perineum that we felt could be blamed on activity.

TABLE XXIX

*Uterine Prolapse and Pelvic Floor Damage at 6th Week*

| Condition | Primiparae | Multiparae | Total |
|---|---|---|---|
| Slight cystocele | 2 | 12 | 14 |
| Slight rectocele | – | 2 | 2 |
| Slight cystocele and rectocele | – | 2 | 2 |
| Cystocele 1-plus | – | 14 | 14 |
| Rectocele 1-plus | – | 3 | 3 |
| Cystocele 1-plus: rectocele 1-plus | – | 20 | 20 |
| Marked cystocele | – | 1 | 1 |
| Cystocele 3-plus: rectocele 1-plus | – | 1 | 1 |
| Uterine descent 1-plus | – | 8 | 8 |
| Uterine descent 2-plus | – | 1 | 1 |
| Total | 2 | 64 | 66 |

*Toilet Privileges and Perineal Care*

Over the years we have gradually reduced the interval between labour and going to the toilet. It has been our policy for some years now to allow the woman to go to the toilet as soon as she will. This is the day after the baby is born in all but a very small number of cases. If the bowels move the patient cleans herself with toilet paper. Once a day the perineum is washed off with dilute green soap solution but this is not done in any definite relation to the time the bowels move. It is our experience that, no matter how deep the episiotomy or tear, faecal matter smeared over it the day after it has been sewn up does not interfere with healing or cause infection or breakdown. In our cases therefore the perineum is washed off daily not for healing but for its cleansing and aesthetic effect. We were led to the conclusion therefore that the complicated perineal care we had previously given our patients was more or less a mumbo-jumbo tribute to the Surgical Rite, and in no way based on the likelihood of keeping sterile, or increasing the rate of healing in this bacteria-swarming locality. We feel that the early permission to go to the toilet and the freedom from perineal care have done a great deal to endear the active regime to our women.

*Embolism*

One of the arguments brought against the active regime was that it would increase the incidence of embolism. We had only 1 case of embolism in our 2,632 cases, a non-fatal mild pulmonary embolism that occurred after the patient had left hospital. While the figures for the incidence of embolism in women undergoing a non-active puerperium vary with different writers, about 1 in 1,500 seems to be that generally accepted. Klein (quoted in Davis) reported 2,524 healthy puerperal patients who sat up in a chair from 1 to 3 days after delivery without a single case of embolus, and Shaw and Rickards (1938), in a total of 5,253 post-operative cases, found that the incidence of embolus was 5 times greater without than with post-operative exercises. We feel that we can safely say that early activity does not increase the tendency to embolism.

*Incidence of Trichomonas Vaginalis in Puerperal Women*

We did rather hurried and slapdash wet smears on 537 of our women at the 10th day, and were somewhat surprised to find trichomonads present in 119 or 22.2 per cent. In only a very small number was there any history of previous symptoms. The organism was found in all types of lochia.

*Attitude of Women Towards Activity*

In seeking to ascertain this we ourselves refrained from asking the question and got the charge nurse to do so, since we felt that the patients might tend to tell us what they thought we wanted to hear, whereas they would speak more frankly to another woman.

*Attitude of the Women Towards Early Ambulation*

We asked all patients at the 10th day, 6th week and in the 3-month questionnaire, how they had liked early ambulation. The multiparae were asked for a comparison with previous puerperia, and the primiparae were asked to compare how they felt on the 10th day with how they felt during the later weeks of pregnancy. The results are shown in Tables XXX, XXXI and XXXII.

It will be noticed that, while there is a falling off in liking on reflection the great majority were in favour of activity. It was the impression of the nurses, who were in a position to compare the general attitude of those undertaking activity with those who were not, that the active women were a happier and better-adjusted group, their outlook more optimistic and sanguine.

## The Final Questionnaire

One thousand one hundred and eighteen women, of whom 451 had been primiparae, and 667 multiparae, answered the questionnaire sent them in 1950; of these 77.6 per cent were delivered between 1928–45 inclusive: in about 50 per cent of the total cases 10 years or more have elapsed—a sufficient time for any late sequelae to arise that might justly be blamed on activity.

TABLE XXX
*Attitude at 10th Day and at 6 and 12 Weeks*

| Attitude | At 10th day | | At 6 and 12 weeks | |
|---|---|---|---|---|
| | No. | Per cent distribution | No. | Per cent distribution |
| Liked | 1792 | 93.1 | 739 | 88.0 |
| Indifferent | 71 | 3.7 | 48 | 5.7 |
| Did not like | 62 | 3.2 | 53 | 6.3 |
| Total | 1925 | 100.0 | 840 | 100.0 |

TABLE XXXI
*Comparison Rate at 6 and 12 Weeks of Multiparae with Previous Inactive Puerperia*

| Attitude | At 10th day | | At 6 and 12 weeks | |
|---|---|---|---|---|
| | No. | Per cent distribution | No. | Per cent distribution |
| Recovered more quickly | 422 | 77.4 | 265 | 59.5 |
| No difference | 105 | 19.3 | 116 | 26.1 |
| Recovered less quickly | 18 | 3.3 | 64 | 14.4 |
| Total | 545 | 100.0 | 445 | 100.0 |

TABLE XXXII
*Attitude of Primiparae at 10th Day Compared with How They felt During Later Months of Pregnancy*

| Feeling at 10th day | Number | Per cent distribution |
|---|---|---|
| Stronger than | 38 | 8.0 |
| No difference | 324 | 68.4 |
| Weaker than | 98 | 20.7 |
| Much weaker than | 14 | 2.9 |
| Total | 474 | 100.0 |

In the questionnaire we attempted to discover the following: (1) Present complaints possibly attributable to early ambulation, (2) incidence of prolapse, (3) number of pelvic operations done subsequently, (4) present attitude towards early ambulation. All references backwards in women with more than one active regime are to the findings at the last active regime. After receiving the replies we traced these women back through the various previous enquiries to see if there was any correlation between any complaints or disabilities they had as of 1950 and the findings at those previous examinations.

*Present Complaints*

Fifty women blamed the active regime for certain complaints they have suffered or are now suffering (see Table XXXIII). Of these only 24 still have (1950) the complaints. Six of these women had the same complaints at the 6th week or 3rd month investigation. The 2 with falling of the womb were found to have some form of prolapse, and are being considered under that category. Of the 24 women now having complaints we were able to trace 13 back to the 10th day examination and 9 to the 6th week examination (see Table XXXV). It will be seen that

TABLE XXXIII
*Ill Effects Blamed on Early Rising by Women Answering Recent Questionnaire*
(Total women answering questions 1,118)

| Complaint | Total | Still present |
|---|---|---|
| Weakness, dizziness, tiredness, etc. | 13 | 4 |
| Backache | 11 | 4 |
| Abdominal pain | 10 | 9 |
| Pain in legs | 3 | – |
| Irregular bleeding | 3 | 1 |
| Pain in back and abdomen | 2 | 1 |
| Bearing down feeling | 4 | 3 |
| Bladder symptoms | 2 | 1 |
| Inflammation | 1 | – |
| Ruptured navel | 1 | 1 |
| Total | 50 | 24 (2 per cent) |

TABLE XXXIV

*Complaints still present among those with Complaints at 6th week or 3rd Month*

| Complaints at 6th week or 3rd month | No. with complaints at 6th week or 3rd month | No. answered recent quest. | No. with complaint still present |
|---|---|---|---|
| Backache ... ... | 38 | 20 | 2 |
| Pain in abdomen | 20 | 11 | 4 |
| Pain in abdomen, backache ... | 6 | 4 | – |
| Tiredness, weakness, dizziness ... ... | 22 | 15 | – |
| Discharge ... ... | 9 | 6 | – |
| Discharge, backache | 1 | 1 | – |
| Menorrhagia ... | 5 | 4 | – |
| Nervousness ... | 5 | 3 | – |
| Headaches ... ... | 4 | 4 | – |
| Falling of womb ... | 2 | 2 | 2 |
| Pain in vagina ... | 1 | 1 | – |
| Haemorrhoids ... | 9 | 6 | – |
| Breast abscess ... | 2 | 2 | – |
| Total ... ... ... | 124 | 79 | 8 |

TABLE XXXV

*Recent Complaints and 10th Day and 6th Week Examinations*

| Size and position of uterus and character of lochia | 10th day | | 6th week | |
|---|---|---|---|---|
| Size | | | | |
| Large ... ... ... | 4 | | 2 | |
| Medium ... ... | 2 | | – | |
| Small ... ... ... | 7 | | 5 | |
| | —13 | | —7 | |
| Lochia | | | | |
| Rubra ... ... ... | – | | | |
| Serosa ... ... ... | 6 | | | |
| Alba ... ... ... | 6 | | | |
| Absent ... ... ... | 1 | | | |
| | —13 | | | |
| Profuse ... ... | 2 | | | |
| Moderate ... ... | 2 | | | |
| Scanty ... ... ... | 8 | | | |
| Absent ... ... ... | 1 | | | |
| | —13 | | | |
| Retroverted ... ... ... | 1 | | 3 | |
| Anteverted ... ... ... ... | 12 | 13 | 4 | 7 |
| Number of patients answering questionnaire | 24 | 13 | | 7 |

these patients at those times had all sizes of uterus (except medium at 6th week) and all types of lochia at the 10th day except rubra and that the uterus had been retroverted in some and anteverted in others. In effect, in so far as these complainers were concerned, large uteri at the 10th day or 6th week (? subinvolution) were not as common as small; nor was retroversion as common as anteversion. We feel, therefore, that neither largeness of the uterus, nor profuse coloured lochia, nor retroversion could be claimed to have played any unusual part in the background of this small group.

We have a number representing 4.4 per cent of those answering the final questionnaire who, to their own way of thinking, developed these varying symptoms as a result of early activity.

*Prolapse*

In addition to the above, 49 cases complained of some degree of prolapse, of which 7 were found on recent examination by us not to have any degree of it and 5 hospital records were found in which, despite the patients' complaint of prolapse, no degree of it was discovered on examination by other men. Seven cases had had prolapse before they undertook early ambulation for the first time.

Thus, of the 1,118 women under consideration who, in so far as we could ascertain, did not have prolapse before early ambulation, 30, or 2.7 per cent, of whom 21, or 1.9 per cent, came to operation, later developed it (see Table XXXVI). This does not seem a high percentage. Although we have searched the literature for comparable figures on the late incidence of prolapse following childbirth we have been unable to find any. The figures given by Salmond and Dearnley (1935) and Nelson and Abramson (1941) are for prolapse occurring within a relatively short time after delivery.

Did so-called subinvolution play any part in the production of prolapse in these 30 cases? Although there is a very slightly greater percentage of ultimate prolapse among those with a large than a medium or small uterus (see Table XXXVII) as found at the 10th day—the difference as between large and small being actually less than 1 per cent—in actual numbers more of the prolapse cases had a small uterus

TABLE XXXVI
*Operations for Prolapse by Years*

| Operation | 1928–34 | 1935–45 | 1947–49 | Total |
|---|---|---|---|---|
| Hysterectomy | 0 | 1 | 0 | 1 |
| Hysterectomy and repair | 2 | 7 | 0 | 9 |
| Repair | 1 | 8 | 1 | 10 |
| Suspension | 0 | 1 | 0 | 1 |
| Total | 3 | 17 | 1 | 21 |
| Total number of cases 1118 | 0.26 per cent | 1.6 per cent | 0.09 per cent | 1.9 per cent |

TABLE XXXVII
*Size of Uterus at 10th Day and Prolapse Later*

| Size of uterus at 10th day | Number of women answered recent questionnaire | Prolapse later | Per cent prolapse later |
|---|---|---|---|
| Large | 144 | 5 | 3.5 |
| Medium | 243 | 5 | 2.0 |
| Small | 395 | 11 | 2.8 |
| Not examined | 336 | 9 | 2.7 |
| Total | 1118 | 30 | 2.7 |

at that time (11 to 5) than had a large or medium. Eight of the 30 prolapse cases were examined at the 6th week and at that time 4 had a medium, 4 a small and none a large uterus. Turning to character of the lochia (see Table XXXVIII) we found that 2 had rubra, 14 serosa, and 3 alba; the incidence of late prolapse in women who at the 10th day had a large uterus and lochia rubra was 3.8 per cent, a large uterus and lochia serosa 3.8 per cent, a large uterus and lochia alba 2.8 per cent. Using the character of the lochia therefore as an expression of subinvolution it would appear that this factor played no greater part than "largeness" of the uterus in predisposing to or causing prolapse in later years.

It would seem fair to conclude that, in so far as our findings go, subinvolution, as referring to largeness or profusion of the lochia, was not productive of prolapse.

Did the number of times a woman undertook early ambulation play any part in increasing the tendency to prolapse? We had 144 repeaters, of whom 104 answered the recent questionnaire, among whom there was only 1 case of prolapse (see Table XXXIX). We have therefore no evidence that repetition of activity increases the tendency to prolapse.

Did retroversion play any part in producing prolapse? We followed these prolapse cases back through the 6th week to the 10th day examination (see Table XL).

Only 1 of the 21 examined on the 10th day had a retroverted uterus at that time, and none of the 13 examined at the 6th week. We have

TABLE XXXVIII
*Size of Uterus and Colour of Lochia at 10th Day and Prolapse Later*

| Size of uterus at 10th day | Rubra | | | Serosa | | | Alba | | | Absent | | | Not examined | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. quest. | Prolapse | Per cent | No. quest. | Prolapse | Per cent | No. quest. | Prolapse | Per cent | No. quest. | Prolapse | Per cent | No. quest. | Prolapse | Per cent | No. quest. | Prolapse | Per cent |
| Large | 26 | 1 | 3.8 | 80 | 3 | 3.8 | 36 | 1 | 2.8 | 2 | – | – | – | – | – | 144 | 5 | 3.5 |
| Medium | 31 | – | – | 126 | 3 | 2.4 | 82 | 1 | 1.2 | 4 | 1 | 25.0 | – | – | – | 243 | 5 | 2.0 |
| Small | 22 | 1 | 4.5 | 204 | 8 | 3.9 | 165 | 1 | 0.6 | 4 | 2 | 25.0 | – | – | – | 395 | 11 | 2.8 |
| Not examined | – | – | – | – | – | – | – | – | – | – | – | – | 336 | 9 | 2.7 | 336 | 9 | 2.7 |
| Total | 79 | 2 | 2.5 | 410 | 14 | 3.4 | 283 | 3 | 1.1 | 10 | 3 | 33.3 | 336 | 9 | 2.7 | 1118 | 30 | 2.7 |

TABLE XXXIX

*Number of Active Regime Puerperia and Prolapse Later*

| Active regime puerperia | Number answered recent questionnaire | Prolapse cases | Recent prolapse per cent |
|---|---|---|---|
| 1 | 1014 | 29 | 2.8 |
| 2 | 90 | 1 | 1.1 |
| 3 | 10 | – | – |
| 4 | 2 | – | – |
| 5 | 1 | – | – |
| 6 | 1 | – | – |
| Total | 1118 | 30 | 2.7 |

uterus is so low in the pelvis that its fundus often lies between ante- and retroversion and combine the first and second degree cases in which retroversion would be likely to be found if it were a factor in producing prolapse. The percentage of retroversion in this combined group is 27 per cent—a figure that lies well within the normal incidence of retroversion among women. Even in first degree prolapse the percentage is only 32.8 per cent, which is within the extremes of that incidence as reported by Moses (35 per cent) and others. We feel that none of our findings supports the following statement of Novak (1948): "What has been

TABLE XL

*Late Prolapse According to Position of Uterus at 10th Day and 6th Week*

| At 10th day | | At 6th week | | | |
|---|---|---|---|---|---|
| | | Retroverted | Anteversion | Not examined | Total |
| Retroversion ... ... | 1 | – | – | 1 | 1 |
| Anteversion ... ... | 20 | – | 10 | 11 | 21 |
| Not examined ... ... | 9 | – | 3 | 5 | 8 |
| Total ... ... ... ... | 30 | – | 13 | 17 | 30 |

therefore no evidence that retroversion, either at the 10th day or the 6th week predisposed to prolapse.

In order to make a check on this finding we went back over 200 consecutive cases presenting themselves at our gynaecological service with some demonstrable degree of prolapse to discover how many of them had an accompanying retroversion (see Table XLI). For this purpose we divided prolapse into the usual first, second and third degree categories. The percentage of retroversion in all cases was 22.5 per cent. Let us eliminate the third degree cases, where the

TABLE XLI

*Retroversion in Prolapse Cases Requiring Operation*

| Degree | No. of cases | Retroversion | Per cent retroversion |
|---|---|---|---|
| 1st | 73 | 24 | 32.8 |
| 2nd | 83 | 19 | 22.8 |
| 3rd | 44 | 2 | 4.5 |
| Total | 200 | 45 | 22.5 |

said as to the causes of the acquired puerperal types of retrodisplacement will apply to the etiology of prolapse. As a matter of fact, most cases of the latter are preceded or accompanied by retrodisplacement of the uterus", or this one from Janney (1950): "There is another consideration, however, which becomes increasingly important as the patient advances in years. It is well recognized that most cases of falling of the womb are preceded by retroversion and that the retroverted position of the uterus predisposes toward prolapse. It may, therefore, be advisable in the third or fourth decade to suspend such uteri to prevent or to treat early prolapse when no treatment was previously necessary for the retroversion *per se* because of lack of symptoms". Our findings present no clear cut evidence that retroversion predisposes to or is unduly associated with uterine prolapse.

*Pelvic Operations*

In addition to the 21 patients operated on for prolapse 56 of our women had to have some

other operation on the pelvic organs (see Table XLII).

Of the above operations only three categories are likely to have been influenced by the type of puerperium the women endured, namely, the hysterectomies, the D. & C.s and the suspensions. The two suspensions listed in Table XLII were done for sterility (in neither case did the woman become pregnant) and the suspension done in Table XXXVI was for prolapse (the uterus was not retroverted). Of the 4 curettages, 3 were done for incomplete abortion ocurring in all cases more than a year subsequent to the active regime and 1 was done for chronic cervicitis. This leaves us with the 40 hysterectomies including the Caesarean hysterectomy listed in Table XLII, and the 10 listed in Table XXXVI to lay at the door of early ambulation. Although bleeding was a symptom in only 35 of the 40 hysterectomies in Table XLII, and the 10 done as part of a Mayo repair, we have traced all 50 hysterectomies back to the 10th day and 6th week examination to determine if so-called subinvolution, as evidenced either by a large uterus or a profuse red lochia, had predisposed these women to bleeding. Thirty-six of the 50 were examined on the 10th day, and the uterus was found to be large in 6, medium in 14 and small in 16: at the 6th week examination we encountered 25 of them of whom 4 had a large, 9 a medium and 12 a small uterus (see Table XLIII). At the 10th day in the 36 women examined the lochia was only profuse and red in one case (see Table XLIV), it was only profuse and with any colour in 6, and it was only rubra in 3 of the cases. We therefore can find no evidence that subinvolution, as generally defined in the textbooks, played any part in predisposing to hysterectomy in our series. We feel that we should emphasize this point since certain textbooks still state that so-called subinvolution predisposes to menorrhagia.

*The Summing up on Subinvolution*

All through this study we have attempted to establish among our cases a clinical entity approximating the "large, boggy uterus that bleeds on the slightest provocation" and that travels under the name of Subinvolution in the textbooks. We have been unable to do so. We cannot establish either that the large uterus (either at 10 days or 6 weeks) is a rogue uterus, or that this large uterus, whether or not associated with a profuse red lochia, predisposes to prolapse, retroversion, or menorrhagia—all of which conditions the textbooks claim it does. Does this mean that early ambulation has caused this entity to disappear entirely from our series? Enthusiastic as we are about activity we have not the temerity to claim that. Which means that we are forced to conclude that either (1) there is no such entity as subinvolution, or (2) if it does occur it leads to no subsequent ill effects. Hendry and Goodwin (1951) state that the following conditions cause subinvolution: "Uterine infection and other pelvic inflammatory disease not necessarily acute in character; retained portions of placenta and membranes; placental or fibrinous polypi; lacerations of the cervix followed by low-grade infection; uterine displacements; all conditions causing chronic pelvic congestion among which

TABLE XLII

*Number of Pelvic Operations Excluding Repairs*

| Operation | 1928–34 | 1935–45 | 1947–49 | Total |
|---|---|---|---|---|
| Hysterectomy | 5 | 32 | 2 | 39 |
| D. & C. | 0 | 3 | 1 | 4 |
| Pre-sacral sympathectomy | 0 | 1 | 0 | 1 |
| Repair of recto-vaginal fistula | 0 | 1 | 0 | 1 |
| Suspension | 0 | 2 | 0 | 2 |
| Ovarian cyst | 0 | 3 | 0 | 3 |
| Cauterization cervix | 0 | 3 | 0 | 3 |
| Ectopic | 0 | 2 | 0 | 2 |
| Caesarean hysterectomy | 0 | 1 | 0 | 1 |
| Total | 5 | 48 | 3 | 56 (5 per cent) |

TABLE XLIII

*Size of Uterus at 10th Day and 6th Week and Hysterectomy Operation Later*

| Size of uterus at 10th day | Size at 6th week: Large | | | Medium | | | Small | | | Not examined | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. quest. | Operation | Rate Per cent | No. quest. | Operation | Rate Per cent | No. quest. | Operation | Rate Per cent | No. quest. | Operation | Rate Per cent | No. quest. | Operation | Rate Per cent |
| Large ... ... ... | 2 | 1 | 50.1 | 8 | – | – | 26 | 1 | 3.8 | 108 | 4 | 3.7 | 144 | 6 | 4.2 |
| Medium ... ... | 4 | – | – | 30 | 3 | 10.0 | 43 | 3 | 7.0 | 166 | 8 | 4.8 | 243 | 14 | 5.8 |
| Small ... ... ... | 4 | – | – | 30 | 3 | 10.0 | 82 | 5 | 6.1 | 279 | 8 | 2.9 | 395 | 16 | 4.0 |
| Not examined ... | 12 | 3 | 25.0 | 50 | 3 | 6.0 | 101 | 3 | 3.0 | 173 | 5 | 2.9 | 336 | 14 | 4.2 |
| Total ... ... ... | 22 | 4 | 18.2 | 118 | 9 | 7.6 | 252 | 12 | 4.8 | 726 | 25 | 3.4 | 1118 | 50 | 4.5 |

TABLE XLIV

*Character of Lochia at 10th Day and Hysterectomy Operation Later*

| Amount of lochia at 10th day | Rubra | | | Serosa | | | Alba | | | Absent | | | Not examined | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. quest. | Operation. | Rate Per cent | No. quest. | Operation. | Rate Per cent | No. quest. | Operation. | Rate Per cent | No. quest. | Operation. | Rate Per cent | No. quest | Operation | Rate Per cent | No. quest. | Operation | Rate Per cent |
| Profuse ... ... | 29 | 1 | 3.4 | 94 | 5 | 5.3 | 19 | – | – | – | – | – | – | – | – | 142 | 6 | 4.2 |
| Moderate ... ... | 33 | – | – | 142 | 6 | 4.2 | 28 | 2 | 7.1 | – | – | – | – | – | – | 203 | 8 | 3.9 |
| Scant ... ... ... | 17 | 2 | 11.8 | 174 | 11 | 6.3 | 236 | 9 | 3.8 | – | – | – | – | – | – | 427 | 22 | 5.2 |
| Absent ... ... ... | – | – | – | – | – | – | – | – | – | 10 | – | – | – | – | – | 10 | – | – |
| Not examined ... | – | – | – | – | – | – | – | – | – | – | – | – | 336 | 14 | 4.2 | 336 | 14 | 4.2 |
| Total ... ... ... | 79 | 3 | 3.8 | 410 | 22 | 5.4 | 283 | 11 | 3.9 | 10 | – | – | 336 | 14 | 4.2 | 1118 | 50 | 4.5 |

may be metinoned enteroptosis and constipation, non-lactation, too-frequent pregnancies; and chronic fatigue and overwork ". All these conditions with the exception of placental and fibrinous polypi were present in our cases. We feel therefore that, if such a condition as subinvolution exists, we should have been able to establish it as a pathological entity, causing the sequelae described in the textbooks. What we did find was that the large uterus, or the uterus with a tendency to a profuse red lochia did not produce any such late sequelae as prolapse, retroversion, or menorrhagia in any significantly greater proportion than the apparently normally involuted uterus. Of course, if a uterus contains a fragment of placenta it will be large and it will bleed but the entity here is not largeness or profuseness of lochia, but the placental fragment, the removal of which brings an end to both signs and symptoms. We wonder, therefore, whether as a clinical entity subinvolution should not be consigned to that limbo to which all but the most timid textbook authors have already sent acute ante-flexion of the uterus.

Haultain and Irvine believe that " involution during the first 10 days of the puerperium was definitely improved by early rising ". Although this is also our impression our own results do not allow us either to confirm or deny it. The reason is that we have been able to find no figures for comparison in the literature on a similar series of women not undergoing early ambulation. All we have is the impression that early ambulation does hasten involution. It would seem as if this were a field warranting further study by those interested in the pursuit of truth, but we feel that if those who undertake such a study are to get anywhere with it, they must all agree on common standards for comparison.

*The Fate of the Retroversions*

Of the 1,118 women who answered the final questionnaire, the position of the uterus at the 10th day and 6th week is shown in Table XLV. Of these women, 391 were examined at the 6th week and 71, or 18 per cent, had a retroverted uterus. We do not know what the present position of their uteri is. As previously stated, no attempt was made at replacement and pessary treatment either at the 10th day or the 6th week in any of these women and only 2 of them had to have any suspension done for a symptom —sterility—thought to be due to retroversion (wrongly, as it turned out). We traced these 2 cases back to the 10th day, when both were anteverted; and to the 6th week, when 1 was retroverted. The operations were done from 4–7 years after the delivery in question.

On the basis that roughly 20 per cent of parous women have a retroverted uterus about 224 of our 1,118 probably had a retroverted uterus at the time of the final questionnaire. The 2 suspensions therefore would represent an incidence of less than 1 per cent. But since suspension is a highly dubious treatment for sterility and one that we have long since given up, we are left with the final conclusion that, despite our failure to correct retroversion at the 10th day or 6th week, none of our women with retroversion either required or benefited from a suspension.

Were there cases that should have had a suspension done? Let us again consider Table XXXIII—the group of women who had symptoms at the time of the final questionnaire for

TABLE XLV

*Position of Uterus at 10 Days and 6 Weeks for Women Answering Recent Questionnaire*

| At 10th day | At 6th week | | | |
|---|---|---|---|---|
| | Retroversion | Anteversion | Not examined | Total |
| Retroversion ... ... ... | 3 | 2 | 27 | 32 |
| Anteversion ... ... ... | 49 | 174 | 527 | 350 |
| Not examined ... ... | 19 | 144 | 173 | 336 |
| Total ... ... ... ... | 71 | 320 | 727 | 1118 |

which no cause was apparent to them beyond early activity. Within the last month we have attempted to discover the position of the uterus among these women but were able to contact only 13. Of these:

3 cases have no symptom now and required no treatment to achieve this. We therefore did not ask them to come for examination.

7 cases with remaining symptoms have an anteverted uterus.

3 cases with symptoms have a retroverted uterus, (1) with stress incontinence and vaginal discharge, (2) with backache and pain in the womb, both of which symptoms seem to be due to a very tender cervix, (3) with an occasional sharp pain in the caecal region. In none of these cases did the symptoms seem due to the mobile retroversion. (This incidence of retroversion—30 per cent—lies within the limits reported in the literature; which means that the number of retroversions is what one would expect.)

Let us assume that all 11 women whom we were unable to contact, in addition to the 3 listed above, have symptoms because their uterus is retroverted. This would yield a figure of 14 in 1,118 women, or 1.2 per cent. Lynch (1922) reports doing 155 suspensions in 1,230 cases, or 12 per cent, where he had previously tried replacement-pessary treatment without success. It would seem, therefore, that such attempts to antevert a retroverted uterus as the knee-chest position and replacement-pessary treatment most decidedly constitute works of supererogation. This is further confirmation of our view, as stated by Perlin (1949), that retroversion, whether puerperal or not, is a normal position of the uterus in those women in whom it occurs, and that, unless complicated by such conditions as pelvic inflammatory disease, endometriosis, or tender prolapsed ovaries causing dyspareunia, it is no more likely to produce symptoms than the anteverted uterus; and that operating on it when it is uncomplicated by such conditions is unlikely permanently to relieve such symptoms commonly blamed on it as backache, menorrhagia, low abdominal pain, sterility, abortion, vaginal discharge, dysmenorrhea, etc. This would seem to be also the impression of Vogt *et al.* (1948), who state that "operation failed to relieve symptoms in three-fourths of the patients". We therefore find ourselves in complete disagreement with the inference to be drawn from such a common textbook statement as the following from the Queen Charlotte's Textbook (1948): "If (puerperal retroversion) is not properly treated, permanent changes may occur in the uterus", and this one from Curtis (1951): "Retrodisplacement of the uterus is an important cause of bleeding". We feel that the results of this study throw sufficient doubt on so much of the textbook teaching on retroversion, that the whole matter should be restudied by others. It may be that our findings do not tell the whole truth and that our experience has been exceptional. But if they approach the truth they seriously undermine the indications on which so many suspensions—still a fairly common operation in some clinics—are done. If they contain any truth at all, it is that we do not yet know why the uterus becomes retroverted puerperally.

*Present Attitude Towards Activity*

Tables XLVI and XLVII show the present attitude of 1,118 women towards early ambulation, and compare it with their attitude at the 10th day and 6th week. It will be recalled that there was a slight falling off in favour at the 6th week especially among those multiparae with previously inactive regimes for comparison. In the case of the latter the favour has been partially restored and now 67.4 per cent of these multiparae feel that they recovered more quickly under the active than the inactive regime. Those answering the question "did they like the regime?" still give an answer of 88 per cent in favour, but of those who were indifferent about it almost all now feel that they disliked it. We are therefore left with a large majority of women favouring the active regime.

## The Summing Up

This study was undertaken in the first place to determine whether or not early ambulation would increase the tendency to subinvolution, ultimate prolapse and embolism. Out of the results obtained we feel justified in claiming the following:

TABLE XLVI
*Attitude at 10th Day, at 6th Week and Recent Questionnaire*

| Attitude | 10th day | | 6th week | | Recent questionnaire | |
|---|---|---|---|---|---|---|
| | No. | Per cent distribution | No. | Per cent distribution | No. | Per cent distribution |
| Liked ... ... ... ... | 1792 | 93.1 | 739 | 88.0 | 989 | 88.5 |
| Indifferent ... ... ... | 71 | 3.7 | 48 | 5.7 | 9 | 0.8 |
| Did not like ... ... ... | 62 | 3.2 | 53 | 6.3 | 120 | 10.7 |
| Total ... ... ... ... | 1925 | 100.0 | 840 | 100.0 | 1118 | 100.0 |

TABLE XLVII
*Attitude Towards Active Regime of Multiparae who also had Inactive Puerperia*

| Attitude | At 10th day | | At 6th week | | Recent questionnaire | |
|---|---|---|---|---|---|---|
| | No. | Per cent distribution | No. | Per cent distribution | No. | Per cent distribution |
| Better ... ... ... ... | 422 | 77.4 | 265 | 59.5 | 491 | 67.4 |
| Same ... ... ... ... | 105 | 19.3 | 116 | 26.1 | 137 | 18.8 |
| Worse ... ... ... ... | 18 | 3.3 | 64 | 14.4 | 100 | 13.7 |
| Total ... ... ... ... | 545 | 100.0 | 445 | 100.0 | 728 | 100.0 |

1. We have no evidence that early ambulation increases the incidence of embolism but rather the contrary.

2. Over a period up to 22 years 2.7 per cent of our patients developed some form of prolapse (uterine descent, cystocele, rectocele). This does not seem a high incidence.

3. If subinvolution is to be diagnosed by largeness of the uterus and profuseness and redness of the lochia, we have no clear evidence either that early ambulation causes it to develop excessively, or that, if it does develop, it predisposes to prolapse, benign uterine bleeding, retroversion, or any other ultimate pelvic pathology.

4. We could find no clear evidence to support the textbook contention that puerperal retroversion is due to (1) relaxation of the supporting ligaments of the uterus, cervix, or vagina, (2) largeness of the uterus, or (3) overdistension of the bladder. Our results would agree with those who hold that puerperal retroversion is not a constant entity and that over the months and years following a confinement the uterus that is anteverted may retrovert and vice versa. Our results would go to support the contention that such measures as the knee-chest position, replacement-pessary treatment, etc., constitute unnecessary meddling, and that suspension is required—if at all—in only an infinitesimal number of cases.

5. Two per cent of our women have ultimate symptoms which they believe due to early ambulation.

6. Almost 90 per cent of our women on mature reflexion state that they liked early ambulation, as against roughly 10 per cent who disliked it. Of the multiparae who had previously inactive puerpera for comparison 67 per cent feel that they recovered more quickly under the active regime.

The follow up work on this study was made possible by funds from a Federal Health Grant.

REFERENCES

Atlee, H. B. (1935): *Canad. Med. Ass. J.*, **33**, 144.
Cornell, E. L., and Mullen, J. J. (1948): *Amer. J. Obstet. Gynec.*, **55**, 768.
Curtis, A. H. (1951): *Textbook of gynecology*. 7th ed. Saunders, Philadelphia.
Davis, C. H. (1951): *Gynaecology and obstetrics*. Prior, Hagerstown, Maryland.
Eastman, N. J. (1950): *Williams' obstetrics*. 10th ed. Appleton Century, New York.
Fischmann, E. W. (1950): *Surg. Clin. N. Amer.*, **30**, 231.

Findley, W. M. (1933): *Amer. J. Obstet. Gynec.*, **26**, 874.

Greenhill, J. P., and DeLee, J. B. (1951): *Principles and practice of obstetrics*. 10th ed. Saunders, Philadelphia.

Haultain, W. F. T., and Irvine, D. J. McI. (1951): *Lancet*, **2**, 607.

Hendry, W. B., and Goodwin, J. C. (1951): *in* Davis (1951).

Janney, J. C. (1950): *Medical gynecology*. 2nd edition. Saunders. Philadelphia.

Lynch, F. W. (1922): *Amer. J. Obstet. Gynec.*, **4**, 362.

Mayes, B. T. (1950). *Textbook of obstetrics*. Australasian Publishing Co., Sydney.

Moir, C. (1932): *Lancet*, **1**, 564.

Moses, S. H. (1939): *Amer. J. Obstet. Gynec.*, **37**, 447.

Nelson, H. B., and Abramson, D. (1941): *Amer. J. Obstet. Gynec.*, **41**, 800.

Novak, E. (1948): *Textbook of gynecology*. 3rd edition. Williams & Wilkins, Baltimore.

Peckham, C. H. (1934): *Bull. Johns Hopk. Hosp.*, **54**, 186.

Perlin, I. A. (1949): *Amer. J. Obstet. Gynec.*, **57**, 959.

*Queen Charlotte's textbook of obstetrics* (1948): 7th edition. Churchill, London.

Salmond, M., and Dearnley, G. (1935): *J. Obstet. Gynaec. Brit. Emp.*, **42**, 446.

Shaw, W. F., and Rickards, C. E. B. (1938): *J. Obstet. Gynaec. Brit. Emp.*, **45**, 451.

Vogt, W. H., and Boedeker, R. V. (1948): *Amer. J Obstet. Gynec.*, **55**, 1044.

# ENDOMETRIOSIS OF THE PLEURA AND OVARIES

BY

JOSEPHINE BARNES, M.A., D.M., M.R.C.P., F.R.C.S., F.R.C.O.G.

*Assistant Obstetrician and Gynaecologist,*
*Elizabeth Garrett Anderson Hospital, London*

THE main sites for extragenital endometriosis have been described many times; most reviews, including those of Macleod (1946) and Goodall (1944), describe spread of the disease as occurring mainly within the abdominal cavity and at or below the level of the umbilicus. Navratil and Kramer (1936) reported the removal of a tumour consisting of endometrial tissue from the right brachio-radialis muscle. Duncan and Pitney (1949) described 2 cases of endometriosis in the thigh. Goodall (1944) mentioned the occurrence of pulmonary metastases in "acute stromatous endometriosis", a condition which exhibits some features of malignant disease, including a tendency to metastasize. Hobbs and Bortnick (1940) showed that endometrium injected intravenously into rabbits passes to the lungs where it remains viable and invades the parenchyma. During pregnancy, endometrial deposits in the lungs become converted into decidua. Small doses of stilboestrol stimulate their growth, though very large doses inhibit them. Vicarious menstruation can occur. The possibility of the existence of ectopic endometrium in the lungs in women was suggested.

No case of endometriosis of the pleura with haemothorax appears to have been recorded until Nicholson (1951) recorded this case from the point of view of the thoracic lesion. I am indebted to him for permission to report it from the gynaecological viewpoint.

## CASE REPORT

Mrs. S., aged 25, was married, and had had no pregnancies.

A haemothorax developed which was aspirated on 4 occasions. The fluid aspirated was red in colour, and one sample was found to contain 10 per cent of haemoglobin. Thoracotomy was performed by Sir Clement Price Thomas; the right lung was covered by a yellowish pedicle which was stripped off. Section of this layer shows typical endometrial tissue.

Gynaecological investigation was made at this point. The patient had been married for 15 months but there had been no sign of pregnancy. Menstruation was normal and regular and there were no gynaecological symptoms. Examination revealed palpable appendages strongly suggesting ovarian endometriosis but no large pelvic mass.

In view of the patient's age, and her desire to become pregnant, it was decided to treat her conservatively. An implant of 200 mg. of testosterone was given, and at this time she returned to Ceylon. Subsequent reports show that testosterone was continued and she remained well for 18 months. Then abdominal pain and irregular uterine bleeding developed. Laparotomy was undertaken at Vellore in South India. The right ovary contained a large haemorrhagic cyst which was adherent to the surrounding intestine. This was removed together with the left ovary which appeared normal. Uterine bleeding recurred one month after this with re-accumulation of fluid in the chest. The patient was advised that if this continued an artificial menopause should be induced with X-rays as the chance of pregnancy was now non-existent.

In spite of this, it seems that conservative treatment was reasonable in the first place as there was still a chance, albeit remote, of pregnancy before the laparotomy. It has been found in the past that pregnancy causes regression or even disappearance of deposits of endometriosis.

## DISCUSSION

The main theories of the origin of endometriosis current at present were summed up by Novak (1947). Sampson first introduced the tubal regurgitation and implantation theory in 1921, but has since modified his views considerably. Meyer and Iwanoff introduced independently the theory of serosal or coelomic metaplasia. Halban believed in spread by lymphatic metastasis and this view was supported by Macleod (1946). Novak (1947) concludes that endometriosis may arise in more than one of these ways.

The occurrence of endometriosis in the pleura, without apparent involvement of the rest

of the lung and with no other apparent lesion elsewhere except in the ovaries, would appear to be explicable only on the basis of metaplasia or heteroplasia occurring in the pleura itself, which it must be remembered is developed originally from the coelomic cavity, and thus has a common origin with the peritoneum.

One interesting point must be noted. Dr. Nicholson pointed out that, in spite of frequent aspirations of bloodstained fluid from the pleural cavity, no fibrin layer had formed on the surface. This can only be explained by the fact that the haemothorax was a form of " vicarious menstruation " and that the fluid, like menstrual blood itself, contained no fibrin.


## Summary

A case is described where a right haemothorax was found to be due to endometriosis of the pleura. Endometriosis of the right ovary was discovered by laparotomy 18 months after an operation for decortication of the affected lung.

The implications of this case in relation to the aetiology of endometriosis are discussed.


## References


Duncan, C., and Pitney, W. R. (1949): *Med. J. Aust.*, **2**, 715.

Goodall, J. R. (1944): *A study of endometriosis.* 2nd edition. Lippincott, Philadelphia.

Hobbs, J. E., and Bortnick, A. R. (1940): *Amer. J. Obstet. Gynec.*, **40**, 832.

Macleod, D. (1946): *Brit. J. Surg.*, **34**, 109.

Navratil, E., and Kramer, A. (1936): *Klin. Wschr.*, **15**, 1765.

Nicholson, H. (1951): *Thorax*, **6**, 75.

Novak, E. (1947): *Textbook of gynecology.* 2nd edition. Saunders, Philadelphia.

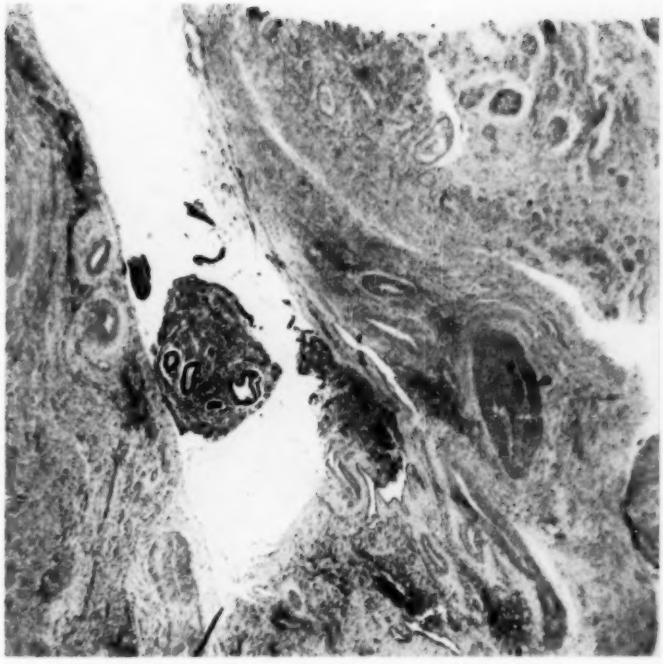


FIG. 1

Low power view of tissue removed from the pleura at operation. An islet of endometrium is seen in the centre. ×28

FIG. 2

Tissue removed from the pleura seen under higher magnification. The typical appearance of endometrium with glands and stroma cells is seen in the centre. ×85

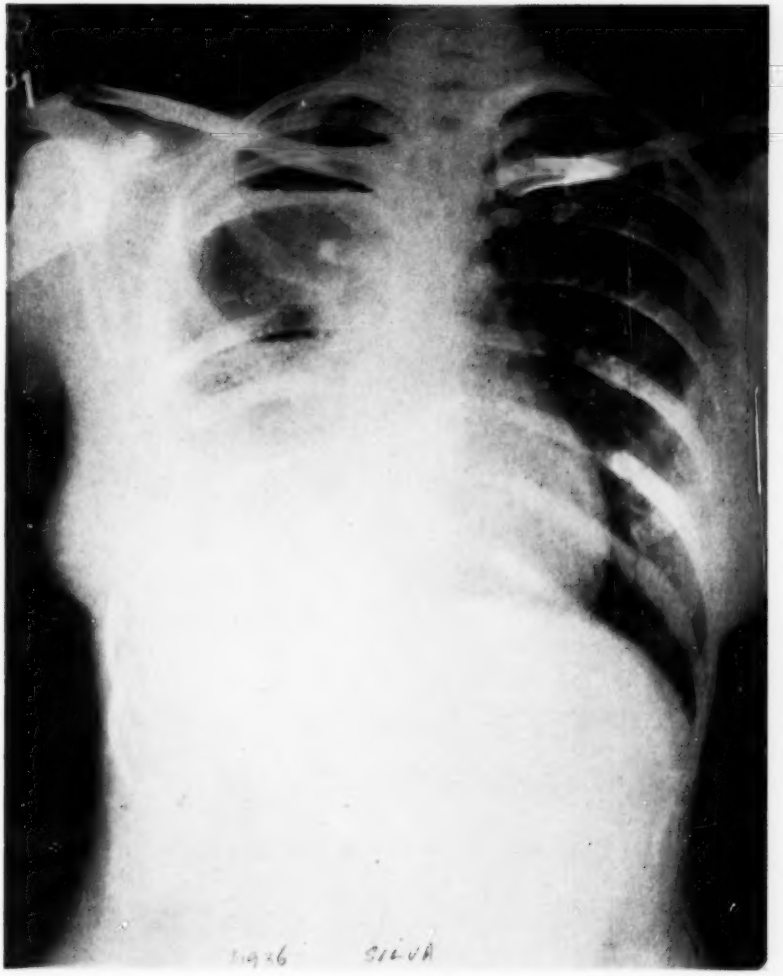


FIG. 3

X-ray of chest showing right haemopneumothorax. The upper margin of the lung is clearly seen and no fibrin deposit on its surface.

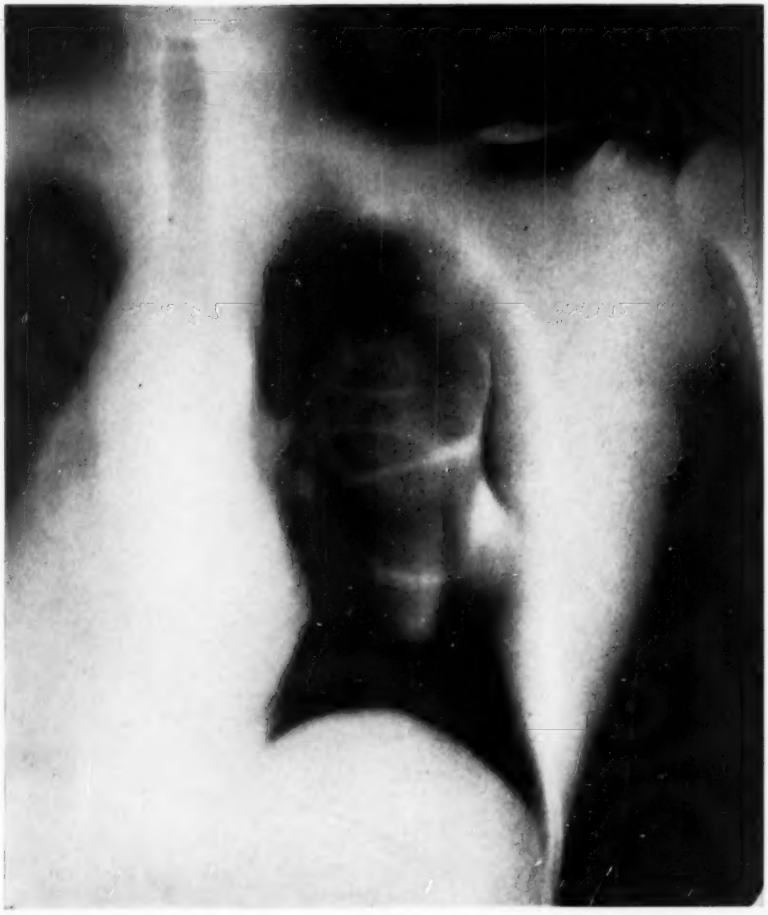


FIG. 4

Tomogram showing appearance of right lung taken from behind. The collapsed lung with the sharp clear margin free from fibrin deposit is seen.

# THE DIAPHRAGM IN THE PUERPERIUM

BY

R. GRENVILLE-MATHERS, M.A., M.D., M.R.C.P.E., F.R.F.P.S.

AND

H. J. TRENCHARD, M.B., M.R.C.P., D.M.R.D.

*Edgware General Hospital, Middlesex*

RESPIRATION is effected by the use of both the intercostal and diaphragmatic muscles. In men the part taken by the ribs in quiet respiration is small, but in women it has been presumed, teleologically, that respiration is predominantly costal, since much excursion of the diaphragm would not be possible during pregnancy. Castleden (1952), as a result of his experience of the measurement of chest expansion in women, considers that such a presumption is not justifiable and there is little doubt that in adults of both sexes normal respiration is achieved principally by diaphragmatic movement.

Our interest in the behaviour of the diaphragm in women arose from the consequences that this may have during pregnancy on a lung affected by tuberculosis. The mechanism by which child-bearing influences the course of tuberculosis has for long been a controversial subject. Although Turner (1950) has postulated that the effects of pregnancy on the disease are in fact due to hormonal changes, it is more often considered that tuberculosis tends to regress during pregnancy because the diaphragm is pushed into the lower thorax by the enlarging uterus, and to progress in the puerperium due to a sudden descent of the diaphragm on delivery. This theory has led Dingle (1944) to advocate the induction of a pneumoperitoneum immediately after delivery.

Stewart (1951), from the examination of routine radiographs in the inspiratory position, has shown that, during pregnancy, there is a small but significant rise in the height of the diaphragm of the order of ½-inch (1.3 cm.). We here report studies of the behaviour of the diaphragm during the puerperium.

## RADIOLOGICAL TECHNIQUE

It was thought necessary to ascertain the height of the diaphragm both in inspiration and expiration. At the beginning of the investigation, which was started some time ago, it was realized that the position and excursion of the diaphragm might vary considerably with posture, and a standard form of radiological technique was necessary in studying changes in the level of the diaphragm. A privately owned Watson MX-2 portable X-ray apparatus was employed. All radiographs taken were antero-posterior with the cassette in contact with the patient's back. The focal spot was 4 feet from the film and was centred 4 inches below the angle of Louis. A double exposure was made, first at the end of deep expiration, and afterwards at the end of deep inspiration. The factors employed were in the range 76 to 80 Kv., 15 MA., for 0.5 sec. for the expiratory exposure, and 65 to 71 Kv., 10 MA., for 0.4 sec. for the inspiratory exposure. Except for certain films taken in the supine position which are described later, all exposures were made with the patient sitting upright with her legs over the side of the bed. To ensure stability, a board was placed across the bed over the mattress to support her weight, and she leaned slightly against a specially made vertical cassette holder placed behind her on the bed.

The resulting radiographs revealed two superimposed images of the chest in expiration and inspiration, and with very few exceptions it was possible accurately to identify the two positions of both domes of the diaphragm. The upper margin of the tip of the 7th right cervical transverse process was found to be practically a fixed point for both exposures. A vertical line

was drawn through the centres of the vertebrae, and other lines were drawn at right angles to it from the upper margin of the tip of of the right 7th cervical transverse process, and from the highest points on the outlines of the domes of the diaphragm in expiration and inspiration. The levels of the diaphragmatic domes were thus measured along the centre line as vertical distances below the level of the transverse process. In a few films identification of the location of a dome of the diaphragm in a particular position could not be made with absolute certainty, and in consequence a few measurements have been omitted as unobtainable.

### Procedure

All the subjects examined were women of child-bearing age (18 to 41). X-rays were taken on admission to the Maternity Unit, when the women were usually early in the first stage of labour, and again as soon as possible after delivery of the placenta—usually 10 to 30 minutes later, although in a few cases there was an interval of several hours before they were X-rayed. Further radiographs were taken 1 week after delivery and at the postnatal examination 6 weeks later. Unfortunately some women failed to attend for postnatal examination and hence this examination had to be omitted in some cases.

### Findings

The position of the highest point of each dome of the diaphragm in 30 women is shown as frequency tables in Tables I and II.

The average fall in the inspiratory position of the diaphragm immediately after delivery was not sufficiently great to be statistically significant, but a week after delivery it was found to be 1.9 cm. below the pre-delivery position on the right side and 1.4 cm. on the left. (This

Table I

*Position of the highest point on the right dome of the diaphragm shown as a frequency table.*

| Position of diaphragm in centimetres | Inspiratory position | | | | Expiratory position | | | |
|---|---|---|---|---|---|---|---|---|
| | Before delivery | Immediately after delivery | 1 week after delivery | 6 weeks after delivery | Before delivery | Immediately after delivery | 1 week after delivery | 6 weeks after delivery |
| 13–13.9 | | | | | 1 | | | |
| 14–14.9 | | | | | 0 | | | |
| 15–15.9 | | | | | 4 | | | |
| 16–16.9 | | 1 | | | 4 | 1 | 1 | |
| 17–17.9 | | 0 | | | 5 | 1 | 1 | 4 |
| 18–18.9 | 3 | 0 | | | 3 | 2 | 2 | 2 |
| 19–19.9 | 4 | 1 | 2 | | 2 | 2 | 3 | 3 |
| 20–20.9 | 5 | 4 | 0 | 2 | 5 | 4 | 6 | 2 |
| 21–21.9 | 3 | 3 | 4 | 3 | 3 | 5 | 0 | 2 |
| 22–22.9 | 6 | 4 | 4 | 4 | 1 | 4 | 7 | 5 |
| 23–23.9 | 3 | 9 | 6 | 3 | 1 | 6 | 1 | 1 |
| 24–24.9 | 2 | 3 | 2 | 5 | | 2 | 1 | 0 |
| 25–25.9 | 2 | 4 | 3 | 0 | | 1 | 1 | 1 |
| 26–26.9 | 2 | 0 | 2 | 2 | | 0 | | |
| 27–27.9 | | 1 | 0 | 0 | | 1 | | |
| 28–28.9 | | | 1 | 1 | | | | |
| 29–29.9 | | | | | | | | |
| Measurement unobtainable | | | 6 | 10 | 1 | 1 | 7 | 10 |
| Mean position (cm.) | 22 | 22.9 | 23.5 | 23.5 | 18.7 | 21.8 | 21 | 20.5 |

Certain measurements were unobtainable owing to inability to identify this point with certainty on a few films. Five women had pneumoperitoneum induced and were not available for some of the after-delivery examinations, and 5 refused to attend for postnatal examinations at 6 weeks. The measurements are vertical distances below the right 7th cervical transverse process as described in the text.

TABLE II

*Position of the highest point on the left dome of the diaphragm*

| Position of diaphragm in centimetres | INSPIRATORY POSITION | | | | EXPIRATORY POSITION | | | |
|---|---|---|---|---|---|---|---|---|
| | Before delivery | Immediately after delivery | 1 week after delivery | 6 weeks after delivery | Before delivery | Immediately after delivery | 1 week after delivery | 6 weeks after delivery |
| 13–13.9 | | | | | | | | |
| 14–14.9 | | | | | | | | |
| 15–15.9 | | | | | | | | |
| 16–16.9 | | | | | 2 | 1 | | |
| 17–17.9 | | 1 | | | 1 | 0 | 1 | 1 |
| 18–18.9 | | 0 | | | 6 | 1 | 1 | 1 |
| 19–19.9 | | 0 | | | 2 | 1 | 1 | 1 |
| 20–20.9 | 2 | 2 | | | 6 | 2 | 3 | 3 |
| 21–21.9 | 5 | 2 | 1 | | 2 | 4 | 2 | 4 |
| 22–22.9 | 3 | 6 | 2 | 6 | 3 | 2 | 1 | 2 |
| 23–23.9 | 5 | 1 | 3 | 3 | 2 | 1 | 3 | 2 |
| 24–24.9 | 4 | 3 | 4 | 4 | 1 | 6 | 6 | 4 |
| 25–25.9 | 2 | 3 | 4 | 1 | | 3 | 2 | 1 |
| 26–26.9 | 3 | 5 | 4 | 2 | | 2 | | 1 |
| 27–27.9 | 3 | 3 | 2 | 1 | | 0 | | |
| 28–28.9 | | 0 | 2 | 2 | | 1 | | |
| 29–29.9 | | 1 | | 1 | | | | |
| Measurement unobtainable | 3 | 3 | 8 | 10 | 5 | 6 | 10 | 10 |
| Mean position (cm.) | 23.8 | 24.3 | 25.2 | 24.8 | 20.2 | 23.1 | 22.5 | 22.0 |

change is twice the standard error of the difference.) On the other hand, the average expiratory position of both hemidiaphragms fell about 3 cm. immediately after delivery (which is significant).

Thus there is an immediate fall in the expiratory position of the diaphragm on delivery and a more gradual fall for the inspiratory position which a week later was found to be about ½-inch below its pre-delivery position, which is comparable with Stewart's (1951) figure for the rise in the inspiratory position during pregnancy. Subsequent films showed that the diaphragm substantially maintained this new position.

We were surprised, however, to find a marked decrease in the respiratory excursion of the diaphragm after delivery. Fig. 1 gives an impression of the results obtained. The difference between the inspiratory and expiratory positions of the diaphragm diminished on the right side from 3.7 cm. before delivery to 1.2 cm. immediately afterwards (5.6 × the standard error of the difference) (Table III). The left side behaved similarly. The excursion of the diaphragm had not returned to its pre-delivery measurement a week after delivery, but appeared to have done so at 6 weeks.

The diminished diaphragmatic excursion was of the same order in primiparae and multiparae. "Bearing down" in labour also did not make any significant difference (Table IV). To test whether the diminished movement immediately after delivery was due to fatigue or paresis of the diaphragmatic muscle, 6 women were X-rayed before and immediately after delivery in the supine position—on each occasion both while horizontal and with the foot of the bed raised 18 inches. Tipping the bed in this way resulted in insufficient upward change in the diaphragmatic position to suggest any marked loss of tone, and it was concluded that fatigue of the muscle was unlikely to be the cause of the diminished respiratory excursion (see Table V).

## MOVEMENT OF THE THORACIC CAGE

We therefore next directed our attention to the movement of the thoracic cage. Wode and

TABLE III
*The excursion of the right hemidiaphragm shown as a frequency table*

| | EXCURSION OF DOME OF RIGHT HEMIDIAPHRAGM | | | |
|---|---|---|---|---|
| Centimetres | Before delivery | Immediately after delivery | 1 week after delivery | 6 weeks after delivery |
| 0–0.4 | | 8 | | |
| 0.5–0.9 | | 8 | 2 | 1 |
| 1.0–1.4 | 2 | 3 | 0 | 2 |
| 1.5–1.9 | 4 | 5 | 5 | 1 |
| 2.0–2.4 | 2 | 1 | 4 | 2 |
| 2.5–2.9 | 2 | 3 | 1 | 2 |
| 3.0–3.4 | 2 | 0 | 4 | 3 |
| 3.5–3.9 | 4 | 1 | 2 | 2 |
| 4.0–4.4 | 4 | | 4 | 2 |
| 4.5–4.9 | 0 | | 0 | 2 |
| 5.0–5.4 | 6 | | 0 | 1 |
| 5.5–5.9 | 2 | | 1 | 0 |
| 6.0–6.4 | 1 | | | 0 |
| 6.5–6.9 | | | | 1 |
| Average (cm.) | 3.7 | 1.2 | 2.8 | 3.2 |

The findings for the left hemidiaphragm were similar, but, owing to difficulty in identifying the level of the left hemidiaphragm in some positions on certain films, the information available concerning its excursion is less complete. By the term excursion is meant the distance between the full inspiratory and expiratory positions of the dome of the diaphragm.

Gilson (1951) found that, on deep inspiration in the erect posture, the upward movement of the thoracic cage lifted the diaphragmatic attachments to such an extent that the dome might occupy a higher level than after a quiet tidal inspiration. As deep expiration and deep inspiration were adopted for the standard method of radiography in these studies, this phenomenon may have affected the measurements but would probably have a similar effect at all X-ray examinations, and therefore was unlikely to have been responsible for the changes noted in the diaphragm.

The X-ray films were not suitable for measuring the transverse diameter of the chest in inspiration but in 14 cases it was possible to measure the expiratory transverse diameter at a level 17 cm. below the 7th cervical transverse process. There was an average decrease of 0.6 cm. in this transverse diameter immediately after delivery and no subsequent change occurred. It was felt, however, that the use of X-ray films to measure changes in the diameter of the chest was not satisfactory since such changes involve small measurements of the order of half a centimetre which are within the possible experimental area, particularly when allowance is made for the distortion inherent in X-ray films. It was, therefore, decided to measure the circumference of the chest with a tape measure.

In a series of 20 patients the chest circumference was measured immediately before and immediately after delivery with the women sitting up in the same position as had been used when X-ray films were taken. The tape measure encircled the chest horizontally immediately below the breasts, this being the only practicable level. Measurements were made in the inspiratory and expiratory positions, in quiet respiration, and after full inspiration and full expiration. With quiet respiration the mean circumference decreased by 3.8 cm. and with full inspiration and full expiration by 2.9 cm. and 4.3 cm. respectively (Table VI). After delivery the excursion of the thoracic cage had increased by 1.4 cm. In the majority of the cases there was little change in the vital capacity before and after delivery. These findings are the reverse of those found in the case of the vertical measurement of the chest as shown by the radiological studies of the diaphragm.

### THE EFFECT OF A PNEUMOPERITONEUM

Finally it was decided to investigate the effect of a pneumoperitoneum on the changes in diaphragmatic movements which had been found to occur after delivery.

In non-pregnant women of child-bearing age it was found that the induction of a pneumoperitoneum raised the level of the domes of the diaphragm both in the inspiratory and expiratory positions and also caused some diminution in the diaphragmatic excursion. These findings were noted on comparing films taken immediately before and after induction of a pneumoperitoneum (Table VII).

A pneumoperitoneum was induced with 1 to 1.5 litres of air immediately after delivery

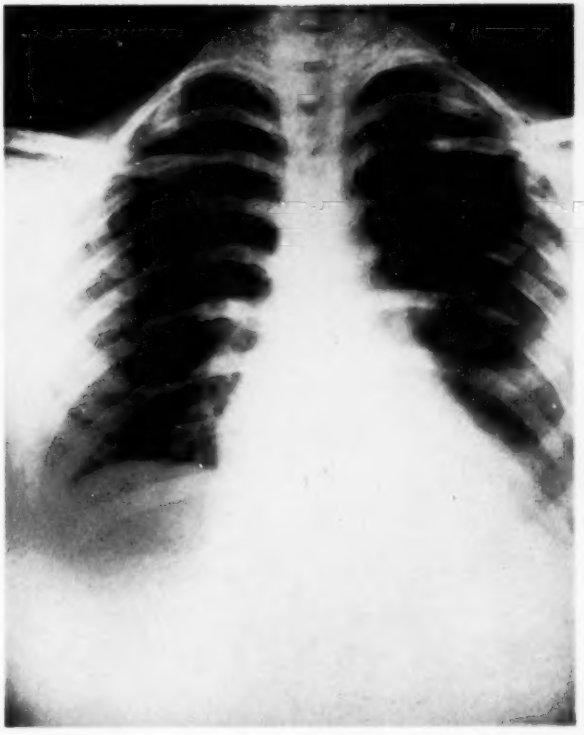


FIG. 1

Double exposure radiograph of a 20-year-old multipara before delivery. The position of the diaphragmatic domes below the level of the upper border of the right 7th cervical transverse process is: right, inspiration 25.2 cm., expiration 21.3 cm.; left, inspiration 27.3 cm., expiration 23.3 cm.

The diaphragmatic excursion is: right, 3.9 cm.; left, 4.0 cm.

TABLE IV

*The excursion of the diaphragm before and immediately after delivery.*

| Excursion of diaphragm in centimetres | EXCURSION OF DIAPHRAGM | | | | | | | | Excursion of diaphragm in centimetres |
|---|---|---|---|---|---|---|---|---|---|
| | Bore down | | | | Did not bear down | | | | |
| | Right | | Left | | Right | | Left | | |
| | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery | |
| 0.0–0.4 | | 1 | | 1 | | 2 | | | 0.0–0.4 |
| 0.5–0.9 | | 2 | | 1 | | 1 | | 2 | 0.5–0.9 |
| 1.0–1.4 | 1 | 1 | | 1 | | 2 | | 1 | 1.0–1.4 |
| 1.5–1.9 | 2 | 1 | | 0 | 1 | 1 | | 2 | 1.5–1.9 |
| 2.0–2.4 | 0 | 0 | 1 | 0 | 0 | 1 | | 0 | 2.0–2.4 |
| 2.5–2.9 | 0 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 2.5–2.9 |
| 3.0–3.4 | 0 | | 0 | | 1 | 0 | 3 | 0 | 3.0–3.4 |
| 3.5–3.9 | 0 | | 0 | | 0 | 1 | 0 | 1 | 3.5–3.9 |
| 4.0–4.4 | 1 | | 0 | | 1 | | 1 | | 4.0–4.4 |
| 4.5–4.9 | 0 | | 1 | | 0 | | 0 | | 4.5–4.9 |
| 5.0–5.4 | 0 | | 0 | | 3 | | 1 | | 5.0–5.4 |
| 5.5–5.9 | 2 | | 2 | | 0 | | | | 5.5–5.9 |
| 6.0–6.4 | | | | | 1 | | | | 6.0–6.4 |
| Mean (cm.) | 3.4 | 1.25 | 4.25 | 1.0 | 4.1 | 1.6 | 3.7 | 1.9 | |

The division into patients who bore down during labour and those who did not was made by the midwifery staff who had no knowledge of the X-ray findings. It was the practice of the midwifery unit to discourage bearing down. There were 6 patients assessed as having borne down and 9 assessed as not having borne down.

Details are not available for all patients as to whether they bore down or not, as this information started to be collected only when the post-delivery diminished diaphragmatic excursion had been discovered in the first cases X-rayed. Owing to certain measurements being unobtainable, information concerning the left hemidiaphragm is not complete.

The difference in the findings between the two groups does not appear to be sufficient to be regarded as significant.

TABLE V

*Position of right hemidiaphragm in cm., in 6 patients X-rayed in supine position, horizontal and tipped with the foot of the bed raised 18 inches.*

| | EXPIRATORY POSITION | | | | INSPIRATORY POSITION | | | |
|---|---|---|---|---|---|---|---|---|
| | Horizontal | | Tipped | | Horizontal | | Tipped | |
| | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery |
| | 16.2 | 18.9 | 16.3 | 17.2 | 19.5 | 20.9 | 19.5 | 19.8 |
| | 19.3 | 20.9 | 20.1 | 20.4 | 21.6 | 21.5 | 22.6 | 21.3 |
| | 17.9 | 18.8 | 17.6 | — | 23.2 | 22.1 | 21.8 | 20.8 |
| | 21.1 | 20.5 | 20.1 | 21.2 | 23.5 | 22.6 | 21.6 | 23.4 |
| | 17.5 | 18.1 | 17.4 | 18.7 | 22.1 | — | 19.1 | 24.6 |
| | 15.1 | 18.2 | 15.5 | 17.8 | 19.2 | 22.0 | 18.6 | 21.5 |
| Mean (cm.) | 17.8 | 19.2 | 17.8 | 19.1 | 21.5 | 21.8 | 20.5 | 21.9 |

The cephalic movement of the diaphragm in the tipped position after delivery is insufficient to suggest paresis of the muscle.

TABLE VI

*The circumference of the chest measured horizontally at a level just below the breasts with the subject sitting upright, showing the measurements just before and after delivery.*

| Primiparae or multiparae | Age | Vital capacity in c.cm. | | CHEST CIRCUMFERENCE IN CENTIMETRES: Average circumference in quiet respiration | | Maximum circumference (inspiration) | | Minimum circumference (expiration) | | Chest expansion | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery | Before delivery | After delivery |
| P. | 33 | 2700 | 2800 | 80.5 | 76.5 | 82 | 80 | 79 | 75 | 3 | 5 |
| P. | 25 | 3100 | 3000 | 80.5 | 77 | 82 | 80 | 79 | 76 | 3 | 4 |
| P. | 29 | 2600 | 1700 | 76.5 | 74 | 78.5 | 76 | 75 | 72 | 3.5 | 4 |
| P. | 20 | 2700 | 1900 | 81 | 80 | 82 | 80 | 80 | 78 | 2 | 2 |
| P. | 18 | 3000 | 2800 | 82 | 78 | 83.5 | 80 | 80.5 | 76 | 3 | 4 |
| P. | 31 | 2700 | 2700 | 79.5 | 75.5 | 80 | 77 | 78 | 73 | 2 | 4 |
| M. | 26 | 2900 | 3000 | 86.5 | 83.5 | 88.5 | 86 | 86 | 83 | 2.5 | 3 |
| M. | 30 | 2500 | 2000 | 86 | 84 | 87.5 | 85.5 | 85.5 | 83 | 2 | 2.5 |
| M. | 37 | 2200 | 2100 | 93 | 90.5 | 94 | 91 | 91.5 | 88 | 2.5 | 3 |
| M. | 34 | 2400 | 2200 | 84 | 79.5 | 85 | 82 | 82 | 77 | 3 | 5 |
| M. | 29 | 2700 | 2400 | 83 | 76.5 | 83.5 | 79 | 82 | 75 | 1.5 | 4 |
| M. | 26 | 3300 | 3500 | 86 | 81 | 87.5 | 83 | 85 | 79 | 2.5 | 4 |
| P. | 41 | 1700 | 1900 | 88.5 | 84 | 89 | 85 | 87.5 | 83 | 1.5 | 2 |
| P. | 29 | 2900 | 3100 | 90.5 | 86 | 92 | 88 | 89 | 84 | 3 | 4 |
| P. | 23 | 2600 | 2600 | 85 | 83 | 85.5 | 83.5 | 84.5 | 81.5 | 1 | 2 |
| P. | 24 | 2800 | 3000 | 93 | 86 | 94.5 | 89 | 92 | 83.5 | 2.5 | 5.5 |
| M. | 22 | 2500 | 2500 | 83 | 80 | 84 | 81 | 82 | 77 | 2 | 4 |
| M. | 31 | 3000 | 3200 | 85 | 79 | 86.5 | 84 | 84 | 77.5 | 2.5 | 6.5 |
| M. | 26 | 3000 | 3200 | 86 | 83 | 87.5 | 86 | 85 | 81 | 2.5 | 5 |
| M. | 29 | 3200 | 2700 | 83.5 | 82 | 85 | 84.5 | 81 | 78.5 | 4 | 6 |
| Mean | | 2625 | 2540 | 84.6 | 80.8 | 85.9 | 83.0 | 83.4 | 79.1 | 2.5 | 3.9 |

The first 12 cases were measured immediately after delivery; for the last 8 an interval of about 24 hours occurred between delivery and the time of measurement. It is to be noted that the circumference of the chest decreases and the expansion increases after delivery. In the majority of cases there was little change in the vital capacity.

in 5 patients. It was found that this procedure raised the mean inspiratory position of the diaphragm above the pre-delivery level while the expiratory position was raised almost to the pre-delivery level. The diaphragmatic movement was not changed by this manoeuvre and the average excursion increased during the week after delivery in the same way as it had done in those women in whom a pneumoperitoneum was not induced (Table VIII). These findings suggested that it was possible to counteract the fall in the diaphragmatic level which occurred on delivery by the induction of a pneumoperitoneum and that this pneumoperitoneum had little effect on the gradual recovery of the degree of diaphragmatic excursion during the first week of the puerperium.

## DISCUSSION

The results we report of radiography immediately before delivery and during the puerperium show that the level of the diaphragm falls on parturition, and during the week after. Although the change in the inspiratory level immediately after delivery is not great, the expiratory level of the diaphragm falls immediately on delivery by about 3 cm., and in consequence the respiratory excursion of the diaphragm is very much diminished immediately after childbirth. Although no doubt the diaphragmatic muscle

TABLE VII

*Position of the diaphragm in cm. in 5 non-pregnant women of child-bearing age before and immediately after induction of pneumoperitoneum.*

| | EXPIRATORY POSITION | | | | INSPIRATORY POSITION | | | |
|---|---|---|---|---|---|---|---|---|
| | Right | | Left | | Right | | Left | |
| | Before PP. | After PP. | Before PP. | After PP. | Before PP. | After PP. | Before PP. | After PP. |
| | 18.7 | 18.4 | 20.4 | 20.5 | 23.0 | 21.3 | 25.4 | 23.4 |
| | 21.0 | 20.3 | 20.5 | 19.6 | 23.3 | 21.1 | 22.4 | 20.6 |
| | 19.3 | 18.9 | 19.3 | 19.3 | 23.4 | 20.5 | 24.1 | 21.6 |
| | 19.8 | 18.9 | 22.2 | 21.5 | 23.2 | 21.5 | 24.4 | 23.4 |
| | 25.5 | 23.5 | 25.2 | 22.3 | 27.6 | 25.1 | 27.8 | 25.0 |
| Mean (cm.) | 20.9 | 20.0 | 21.5 | 20.6 | 24.1 | 21.9 | 24.8 | 22.8 |

| | Right | Left |
|---|---|---|
| Average rise of inspiratory position of diaphragm following PP. | 2.2 cm. | 2.0 cm. |
| Average rise of expiratory position of diaphragm following PP. | 0.9 cm. | 0.9 cm. |
| Average excursion of diaphragm before PP. | 3.2 cm. | 3.3 cm. |
| Average excursion of diaphragm after PP. | 1.9 cm. | 2.2 cm. |
| Average diminution of excursion of diaphragm | 1.3 cm. | 1.1 cm. |

may be tired by its use as an auxiliary during labour, it is doubtful whether fatigue plays any great role in causing the diaphragmatic movement to be diminished, because "bearing down" does not appear to be significantly associated with the diminished movement. In the primigravid woman the diaphragm probably has more work to do in labour than in the multiparous, yet there was no significant difference in this series between primiparae and multiparae in the diminished movement after delivery. Furthermore, tipping the foot of the bed, which with a fatigued diaphragm might be expected to produce considerable cephalic movement from pressure by the abdominal viscera, in fact produced no such effect.

It is necessary, therefore, to consider other causes for this restricted diaphragmatic excursion. The diaphragmatic respiratory movement before delivery is quite considerable—larger in fact, although not necessarily significantly larger, than 6 weeks after childbirth—and this considerable excursion occurs in spite of the presence of a gravid uterus. At the sime time the movements of the thoracic cage appear somewhat restricted, and the circumference of the chest is somewhat larger than after delivery. It seems possible that the presence of the fundus reaching to the costal margin impedes expiratory movement of the ribs and that respiration in a pregnant woman at term is, surprisingly, predominantly diaphragmatic and not costal. After delivery the ribs take a larger share in breathing and there is no need for the diaphragm to move so much. This is probably fortunate, because the muscles of the anterior abdominal wall are loose after delivery and may not be very efficient in pushing the diaphragm up on expiration. The expiratory position of the diaphragm is presumably normally achieved by the intra-abdominal pressure due in turn to tone and contraction of the muscles of the abdominal wall.

It is possible to counteract the fall in the diaphragmatic level which occurs on delivery by the immediate induction of a pneumoperitoneum should this be desired. As, however, the full lowering of the diaphragm does not occur immediately, but probably over the course of the first week of the puerperium, and as the anterior abdominal walls are usually lax and flabby after delivery, it would appear that there is no particular advantage to be gained from inducing a pneumoperitoneum immediately and that its postponement for a few days could well be considered.

TABLE VIII

*Position of diaphragm in cm. in 5 cases in whom pneumoperitoneum was induced with 1 to 1.5 litres air immediately after delivery (within 2 hours).*

| | EXPIRATORY POSITION OF DIAPHRAGM | | | | | | | | INSPIRATORY POSITION OF DIAPHRAGM | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Right | | | | Left | | | | Right | | | | Left | | | |
| | Before delivery | After delivery | After PP. | 1 week later | Before delivery | After delivery | After PP. | 1 week later | Before delivery | After delivery | After PP. | 1 week later | Before delivery | After delivery | After PP. | 1 week later |
| | 15.4 | 16.9 | 17.1 | — | 16.3 | 16.5 | 18.0 | — | 20.5 | 19.8 | 19.5 | — | 21.6 | 20.3 | 20.6 | — |
| | 15.4 | 20.9 | 17.0 | 16.8 | 16.4 | 20.2 | 18.2 | 16.4 | 20.6 | 22.4 | 19.5 | 19.7 | 21.7 | 22.8 | 20.5 | 20.2 |
| | 20.6 | 23.2 | 19.8 | — | 20.6 | 24.1 | 20.7 | — | 22.6 | 24.0 | 20.5 | — | 24.3 | 25.1 | 23.8 | — |
| | 20.2 | 23.0 | 17.8 | 20.2 | 19.7 | 25.5 | 22.0 | 22.7 | 23.5 | 23.3 | 18.5 | 22.5 | 23.9 | 27.0 | 24.1 | 25.5 |
| | 17.4 | 24.3 | 19.3 | 17.9 | 18.1 | 21.8 | 18.7 | 18.5 | 21.8 | 25.0 | 20.8 | 22.3 | 20.7 | 22.6 | 19.6 | 22.5 |
| Mean (cm.) | 17.8 | 21.7 | 18.2 | 18.3 | 18.2 | 21.6 | 19.5 | 19.2 | 21.8 | 22.9 | 19.8 | 21.5 | 22.4 | 23.6 | 21.7 | 22.7 |

It is not within the scope of this paper to discuss whether a pneumoperitoneum should be induced after delivery in tuberculous women as a method of treatment of the chest condition. Our investigations do show, however, that the level of the diaphragm does fall in the puerperium and that this fall can be reversed (if thought necessary) by the induction of a pneumoperitoneum.


## Summary

Using a special radiological technique showing the position of the diaphragm in inspiration and expiration, the diaphragmatic level immediately before delivery and during the puerperium has been investigated. It was found that immediately after delivery the diaphragmatic respiratory excursion was very much diminished, and that this tends to recover late in the puerperium. Before delivery breathing seems to be predominantly diaphragmatic, but immediately after delivery there is a relative increase in the costal element of respiration which coincides with the decrease in diaphragmatic respiratory excursion. The level of the diaphragm falls after delivery and during the succeeding week and this fall can, if it is desired, be counteracted by the induction of a pneumoperitoneum.


We are much indebted to Mr. E. ap I. Rosser and to Mrs. Rose for permission to carry out investigations on their patients, and to Miss Gorick, Superintendent of the Midwifery Department, and her staff for their patience and assistance to us during our often prolonged visits to her department at all hours. Our thanks are due to Mr. D. J. Wheeler, B.Sc., for his help with analysis of statistical data.

## References


Castleden, L. I. M. (1952). Communication to Middlesex County Medical Society.

Dingle, P. (1944): *J. Obstet. Gynaec. Brit. Emp.*, **51**, 499.

Stewart, C. J. (1951): *Tubercle*, **32**, 40.

Turner, H. M. (1950): *Lancet*, **1**, 697.

Wode, O. L., and Gilson, J. C. (1951): *Thorax*, **6**, 103.

# THE INFANTS OF DIABETIC MOTHERS

## A Morphological Study

BY

B. S. CARDELL, M.D.
*Senior Lecturer in Morbid Anatomy*
*King's College Hospital Medical School, London*

A VAST literature exists on the subject of pregnancy and diabetes mellitus but there are relatively few observations on the pathological changes occurring in the infants of diabetic mothers. This study is based on the postmortem findings in 25 infants of diabetic mothers. Although a small series it represents material over a period of 5½ years from one of the larger diabetic clinics in Britain. To save repetition the findings and the relevant literature are considered organ by organ.

### MATERIAL

This paper is based upon postmortem material from the following groups of cases:

(1) *Diabetic* group. This consisted of 25 infants of diabetic mothers Sixteen cases were seen personally in the period April 1949 to September 1952 and 9 cases were found in the postmortem records of the previous 2 years.

The gestational age of the infants ranged from 30 to 37 weeks and their weight from 1,300 to 4,950 g. Six were stillborn, 18 died within 24 hours of birth, and 1 died aged 3 weeks. Fifteen were male, 9 were female and 1 was a hermaphrodite. Four infants were macerated.

This group represents 25 pregnancies in 24 women who had been diabetic for periods ranging from 1 to 22 years. All but 2 mothers were well-controlled diabetics and in none did the diabetes improve during pregnancy. The obstetric history ranged from first pregnancies to a woman who had 7 children and 14 miscarriages. Toxaemia was diagnosed in 10 cases and hydramnios in 12. The modes of delivery were as follows: Caesarean section 19, spontaneous stillbirth 5, and artificial rupture of membranes 1.

All the mothers had a negative Wassermann reaction. Only 2 of the mothers were rhesus negative and neither showed any evidence of iso-immunization. Eight mothers had oestrogen therapy from an early stage of pregnancy.

(2) *Control group.* This included material from postmortems performed on 64 infants between April 1949 and September 1952. No infants surviving over 48 hours or cases of erythroblastosis foetalis were included. Thirty-two were stillborn and 32 were liveborn. Their gestational age ranged from 29 to 42 weeks and their weight from 950 to 4,750 g. Forty-one were male and 23 were female.

(3) *Foetuses.* Twenty-one foetuses were examined, including 5 from diabetic mothers. Their gestational age ranged from 14 to 26 weeks and their weights from 21 to 1,100 g.

### EXTERNAL FEATURES

*Weight.* As can be seen from Fig. 1, most of the infants in the diabetic group were heavier than infants of similar gestational age in the control group. Fig. 2 shows a similar diagram for foetuses of less than 28 weeks and, although the number of cases is small, the results suggest that there is no difference in weight between the two groups. It is possible that the factor producing large babies does not operate until some time after the 28th week of pregnancy.

It is generally recognized that many infants of diabetic and of prediabetic mothers are heavier than normal (Peel and Oakley, 1950; Warren and LeCompte, 1952; White, 1952). A prediabetic mother is one who at some time after the pregnancy referred to develops diabetes. The possibility that the increase of weight does not occur until the later part of intra-uterine life

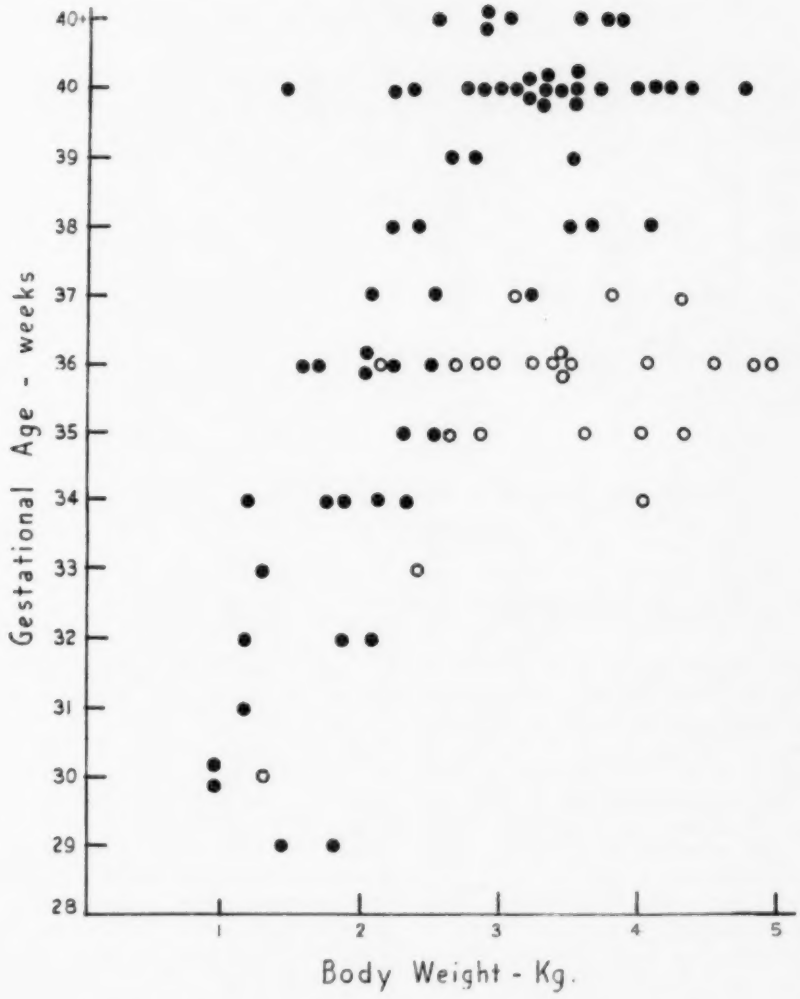



FIG 1
Relation between body weight and gestational age in infants of diabetic (○) and non-diabetic (●) mothers. Gestational age over 28 weeks.

receives some support from the observations of Warren and LeCompte (1952). They found in a series of 43 infants that 8 out of the 13 weighing less than 2,000 g. were below the calculated weight for the recorded gestational age, whilst only 2 out of 30 infants weighing over 2,000 g. were below the calculated weight. White (1952) stated that the body weights of these infants is influenced by three factors; fat, oedema and large size of organs. In the present series no excess of adipose tissue was noted in any infant. The other two factors are discussed later.

*Length.* It was found that the infants in the diabetic group were of greater length than infants

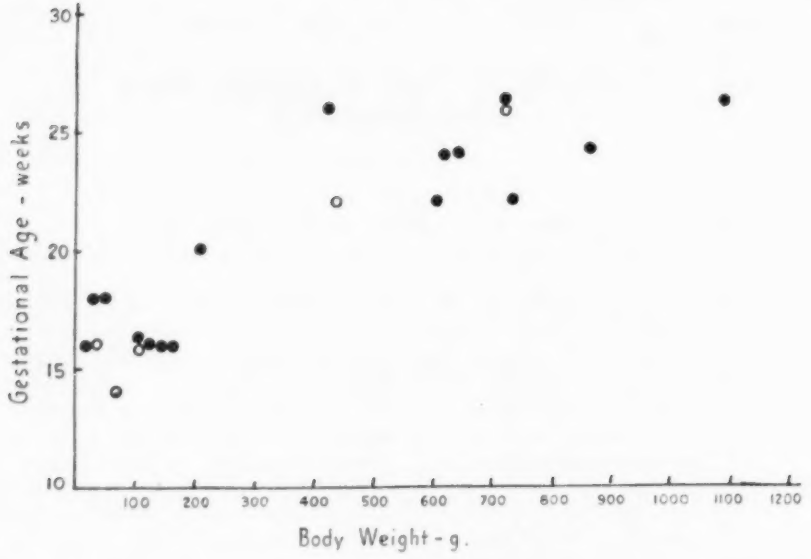



FIG. 2
Relation between body weight and gestational age in foetuses of diabetic (○) and non-diabetic (●) mothers. Gestational age under 28 weeks.

of similar gestational age in the control series. The increase in length was proportional to the increase in weight and the length–weight ratio was the same in both groups of infants (Fig. 3).

Warren and LeCompte (1952) found that the observed length exceeded the calculated length in 25 out of 40 infants. Five were heavier but shorter than the calculated standards and 2 were lighter but longer.

*Oedema.* Only 2 cases in the present series showed mild oedema. Oedema in infants of diabetic mothers has been noted by Miller, Johnson and Durlacher (1944) in 3 out of 10 cases, by Given, Douglas and Tolstoi (1950) in 5 out of 13 cases, and by White (1952). The last author stated that evidence of oedema is also shown by an increased weight loss after birth. She found that in a group of 60 infants of diabetic mothers the average weight loss in 72 hours was 10.5 ounces compared with 6.3 ounces in a control group. The average body weights of these two groups of infants are not stated.

In order to investigate this last finding a number of case records were consulted. Table I shows the results from 71 infants of diabetic mothers, and 730 infants of non-diabetic mothers. Both series are of consecutive case records in which the necessary information was available. The two groups differed in that the average weight in the diabetic series was slightly greater than the control series, and the average gestational age of the diabetic group was less than the control group, as most diabetic mothers had Caesarean section at about the 36th week whilst the control group consisted mainly of full-time pregnancies. In each weight group there is a greater loss in the diabetic series and the loss of weight extended over a longer period. The average weight loss for all the diabetic cases was 8.9 per cent of body weight compared with 5.7 per cent in the control series. This difference would account for only a small part of the increase in weight in infants of diabetic mothers.

*Jaundice.* Jaundice was noted in 1 infant in the present series. It was mild and its cause was not ascertained. Rössle (1942) recorded severe jaundice in an infant dying on the 7th day, but

TABLE I

*Neonatal weight loss in 71 infants of diabetic mothers and 730 infants of non-diabetic mothers.*

| Body weight (pounds) | | Number of infants | Average weight loss (ounces) | Average weight loss (per cent of body weight) | Duration of loss (days) |
|---|---|---|---|---|---|
| 5–6 | Diabetic | 7 | 7.8 | 8.9 | 4.1 |
| | Control | 68 | 4.9 | 5.6 | 4.1 |
| 6–7 | Diabetic | 19 | 7.8 | 7.5 | 4.7 |
| | Control | 187 | 6.1 | 5.9 | 2.6 |
| 7–8 | Diabetic | 17 | 12.2 | 10.2 | 4.6 |
| | Control | 295 | 6.8 | 5.7 | 3.8 |
| 8–9 | Diabetic | 19 | 13.1 | 9.6 | 5.5 |
| | Control | 137 | 7.7 | 5.7 | 3.7 |
| 9–10 | Diabetic | 9 | 12.7 | 8.3 | 4.0 |
| | Control | 43 | 8.3 | 5.5 | 3.3 |
| All weights | Diabetic | 71 | 10.9 | 8.9 | 4.7 |
| | Control | 730 | 6.7 | 5.7 | 3.7 |

autopsy revealed areas of acute hepatic necrosis which were considered to be due to hypoglycaemia. Miller *et al.* (1944) found that jaundice was rare in these infants. White (1946) stated that the jaundice with a normal blood count and no tendency to bleed was found in all cases. Later she modified this view (White, 1952) stating that mild jaundice occurred in many cases prior to 1950, and that with maternal hormone therapy these infants were not jaundiced. Given *et al.* (1950) noted jaundice in 2 out of a series of 13 infants.

That jaundice is uncommon in these infants is now generally accepted. The reason for its occurrence is unknown.

## THE GENERAL ORGANS

*Organ weight.* There are several reports in the earlier literature of visceromegaly in the infants of diabetic mothers. To investigate this point the weights of the various organs in the diabetic group were compared with those in the control group, firstly in relation to the gestational age of the infants and secondly in relation to the body weight of the infants. It should be noted that the figures obtained in the control series were evenly distributed around the average figures recorded by Potter and Adair (1949). It was found in the diabetic group that, when compared with the gestational age of the infants, the organ weights tended to lie towards the upper limit of the normal range and in many cases to exceed it. When compared with the body weight of the infants, however, the weights of most organs lay within the normal range. The detailed findings are discussed under the individual organs.

It is concluded, therefore, that, in general, the increase of organ weight is only apparent and is related to the increase of body weight. In many of the reports of visceromegaly in these infants two errors have been made. Firstly, comparison with average figures for the organ weights instead of with the normal range; and, secondly, comparison with infants of similar gestational age instead of with infants of similar body weight.

*Brain.* The weights of the brains were compared with those observed in infants of similar body weight in the control series (Fig. 4). Of the 15 cases, 5 lay within the lower part of the normal range and 10 were below the normal range. In all these cases the weights were below the average figures for normal infants of similar body weight as recorded by Potter and Adair (1949). No explanation could be found for this observation. In 3 cases there appeared to be an excess of cerebrospinal fluid in the cerebral subarachnoid space. Histological examination of various areas of the brain was

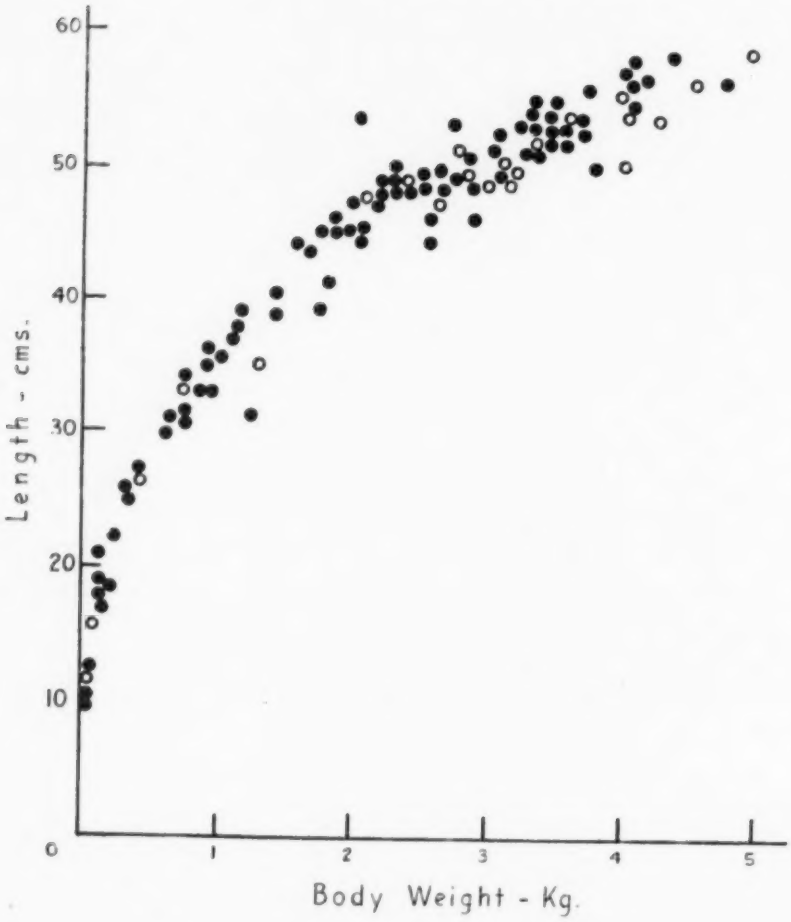



FIG. 3
Relation between length and body weight in infants of diabetic (O) and non-diabetic (●) mothers.

performed in 7 cases. No abnormality was found. A low brain weight has been noted by White and Hunt (1943) in 11 out of a series of 15 infants, and in a later report (White, 1946) it was stated that the weight of the brain did not equal that expected for normal infants in any case.

*Heart.* Fig. 5 shows the weights of the hearts of infants of the diabetic and the control series plotted against their body weight. Four cases lie well above the normal range. Applying the formula of Miller (1944) for heart weight in newborn infants these 4 cases are the only ones to exceed the calculated weight by more than three times the standard deviation. One of these cases was in the control series and no cause for the cardiac enlargement was found. The others were from infants of diabetic mothers. One was an infant of 36 weeks weighing 3,240 g. with a heart weight of 36 g. It had paroxysmal supra-

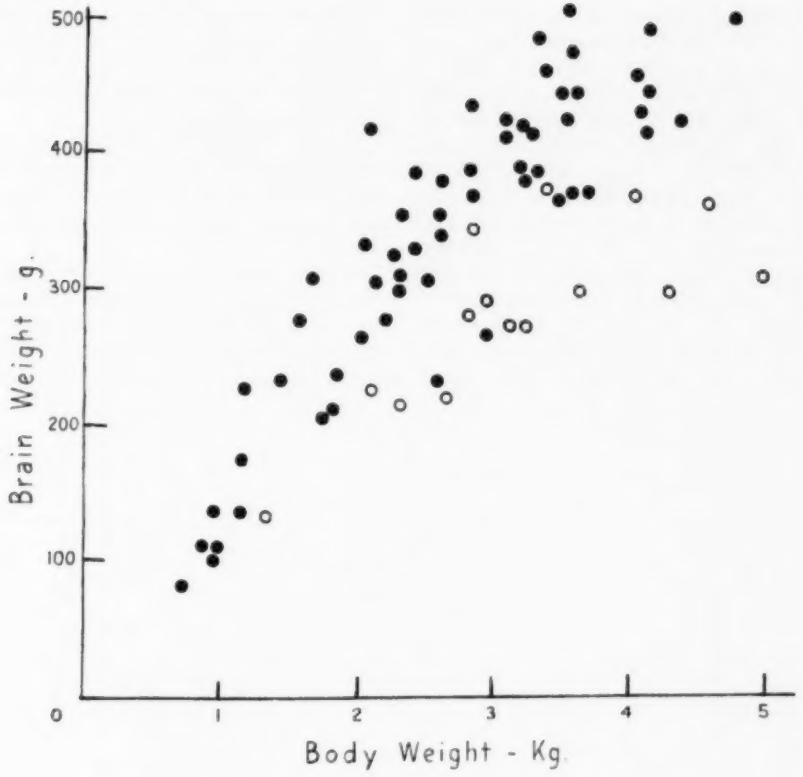



FIG. 4
Relation between brain weight and body weight in infants of diabetic (○) and non-diabetic (●) mothers.

ventricular tachycardia diagnosed *in utero*, with a pulse rate of 240 per minute, and died 7 hours after birth. The next, an infant of 34 weeks, weighing 4,010 g., with a heart weight of 38 g., lived 11 hours; no cause was found for the cardiac enlargement. The third case, an infant of 36 weeks, weighing 4,540 g., with a heart weight of 50 g., lived 21 hours. There was a minute supernumary pulmonary valve cusp, but no other structural abnormality. Sections showed only a small quantity of glycogen in the myocardium. The meningeal vessels were very tortuous and dilated, a finding that Potter (1952) considered responsible for some cases of cardiac hypertrophy.

Glycogen was present in the myocardium in small quantities in 6 out of 10 cases examined in the diabetic group and in 1 out of 4 cases in the control group. Sections stained by Congo red and by methyl violet showed no evidence of amyloidosis.

An increase of heart weight has been recorded by Hurwitz and Irving (1937), Rascoff, Beilly and Jacobi (1938), Miller *et al.* (1944) in 4 out of 10 cases, and also in an infant of a pre-diabetic mother, and by Given *et al.* (1950) in 4 out of 13 cases. Warren and LeCompte (1952), using Miller's formula, found 19 out of 41 cases to exceed the calculated weight by over twice the standard deviation, whilst only 6 out of 70 infants in a control group exceeded this range.

An increase of glycogen in the myocardium has been reported by Hurwitz and Irving (1937), Bayer (1942), Rössle (1942), and in 2 cases by Miller *et al.* (1944). In a further case (Wenig, 1941) the infant had glycogen storage disease. Warren and LeCompte (1952) stated that marked vacuolation of heart muscle fibres is common in these infants and that it is often more striking than in the normal foetal heart which also contains a good deal of glycogen. Chemical analysis was performed in 5 of their cases and 2 showed a high glycogen content.

The present state of knowledge is adequately summed up by Warren and LeCompte (1952), who state that enlargement of the heart is seen frequently enough to be considered significant, and that although it is probable that these hearts contain more glycogen than normal ones the increase in size cannot be entirely due to the glycogen deposition.

*Lungs.* The weights of the lungs were compared with those observed in infants of similar body weight in the control series (Fig. 6). No significant deviation from the normal range was observed.

In the earlier literature there were many reports of atelectasis as a cause of death in the infants of diabetic mothers. Recently attention has been focused upon pulmonary hyaline membrane disease by White (1952), who stated that

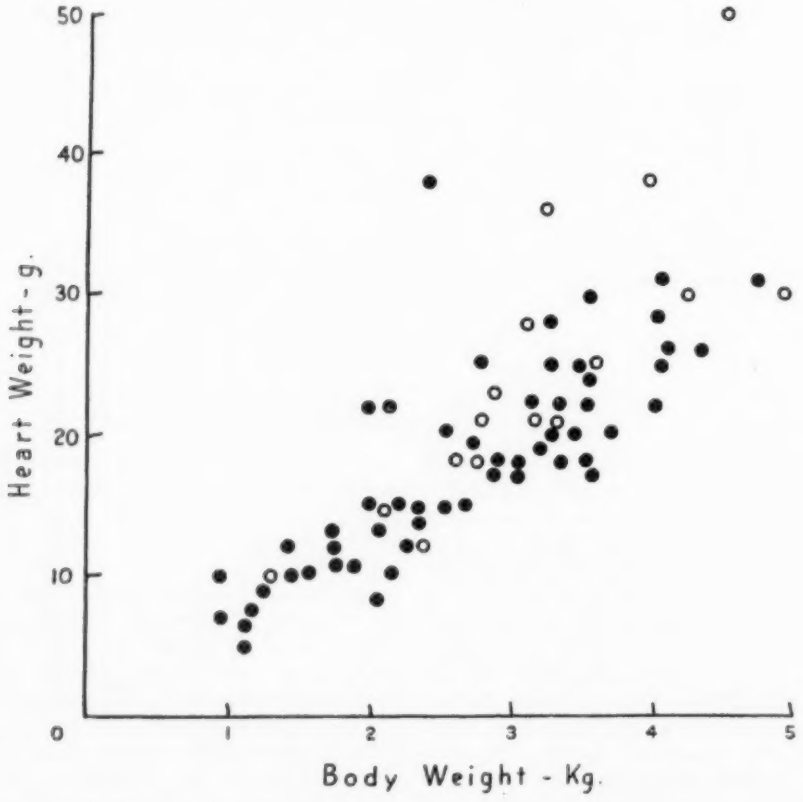



FIG. 5
Relation between heart weight and body weight in infants of diabetic (○) and non-diabetic (●) mothers.

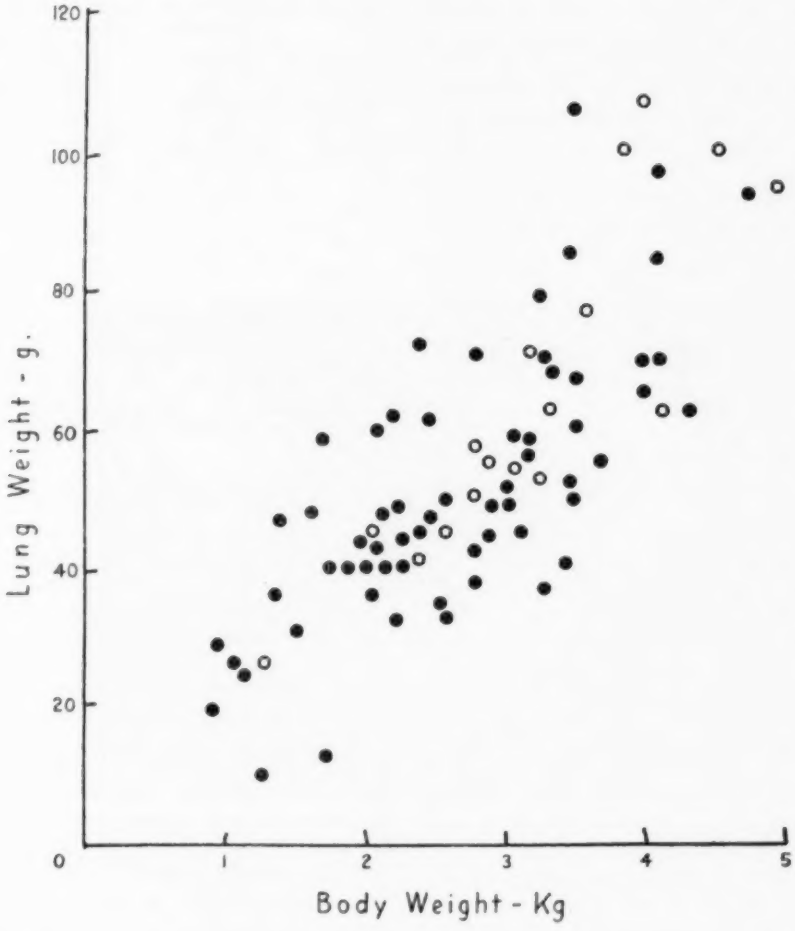



FIG. 6
Relation between lung weight and body weight in infants of diabetic (○) and non-diabetic (●) mothers.

this had been the most constant finding, and by Warren and LeCompte (1952), who gave it as the cause of neonatal death in 8 infants, most of whom were delivered by Caesarean section.

Pulmonary hyaline membrane formation with resorption atelectasis has recently been recognized as an important cause of death in premature liveborn infants (Blystad, Landing and Smith, 1951; Bruns and Shields, 1951; Potter, 1952). The lungs in these cases present a characteristic histological picture. There is intense capillary engorgement and many of the smaller bronchioles and alveolar ducts are lined by a layer of homogeneous acidophilic hyaline-like material; the associated alveoli are collapsed. The origin and nature of this hyaline-like membrane has not yet been fully elucidated, but it is believed to occlude the alveolar ducts,

and secondary atelectasis results from resorption of air from the associated alveoli. Clinically these infants usually breathe spontaneously at birth and for several hours seem normal. Then there is progressive cyanosis and dyspnoea. The breathing becomes extremely laboured and there is retraction of the sternum and ribs with each inspiration.

This condition is not seen in stillborn infants, in infants dying within an hour of birth or in those surviving more than a week. It is rare in infants of under 1,000 g. body weight and uncommon in infants of over 2,500 g. body weight. Most of the larger infants in which this condition has been present have been delivered by Caesarean section, and many of these cases also showed an increase of cerebrospinal fluid in the cerebral subarachnoid space.

In the present investigation the lungs were examined histologically in 13 of the liveborn infants whose gestational age ranged from 34 to 36 weeks, and who survived from 4 to 21 hours. Eleven showed resorption atelectasis with hyaline membrane formation (Fig. 7); only one of these infants weighed less than 2,500 g. One infant who lived 21 hours showed early bronchopneumonic changes. This was the only infant delivered vaginally, and delivery occurred 42 hours after artificial rupture of the membranes. The remaining infant died of heart failure due to paroxysmal tachycardia 7 hours after birth; no hyaline membrane was present in the lung. Hyaline membrane formation was not seen in any of the stillborn infants.

In the control series hyaline membrane formation was not seen in any stillborn infant (10 cases). It was present in 8 out of 9 liveborn infants of 36 weeks or less gestational age and in one of 13 liveborn infants of over 36 weeks gestational age. Only one of the infants with a pulmonary hyaline membrane weighed over 2,500 g.

These findings confirm the importance of resorption atelectasis with hyaline membrane formation as a cause of death in the infants of diabetic mothers. The relative importance of prematurity and of Caesarean section as causal factors in these cases remains to be elucidated.

*Liver.* The weights of the livers were compared with those observed in infants of similar body weight in the control series (Fig. 8). None of the livers appeared to be significantly enlarged.

TABLE II
*Haemopoiesis in liver in infants of diabetic and non-diabetic mothers*

| Degree of haemopoiesis | Diabetic group. Gestational age 30–37 weeks | Control group gestational age | |
|---|---|---|---|
| | | 29–37 weeks | Over 37 weeks |
| + | 1 | 4 | 22 |
| + + | 2 | 6 | 3 |
| + + + | 9 | 4 | 0 |
| + + + + | 2 | 0 | 0 |
| Number of cases | 14 | 14 | 25 |

There was an increased degree of haemopoiesis compared with infants of the same gestational age in the control group (see Table II, and Figs. 9 and 10). Its distribution and character were the same as in normal infants of considerably less maturity. In 2 cases it equalled the maximum normally found in early intra-uterine life.

Haemosiderosis was of a lesser degree than in the control group. It was absent in 11 cases and of slight degree in 2. In the control group of similar gestational age it was absent in 5 cases and slight in 6. This feature is of value in differentiating these infants from cases of erythroblastosis foetalis where haemosiderosis is often considerable (Macklin, 1944).

Vacuolation of the liver cells was of a greater degree than in control infants of similar gestational age, but of similar degree for infants of the same body weight. Specific staining methods showed that the vacuolation was due to the presence of neutral fats. Glycogen was present in small amounts in 4 out 12 cases examined in the diabetic group and in 2 out of 4 cases from the control group.

Enlargement of the liver has been recorded by Dubreuil and Anderodias (1920), Gordon (1936), White and Hunt (1943), and Given *et al.* (1950). Warren and LeCompte (1952) found no significant enlargement in 42 cases.

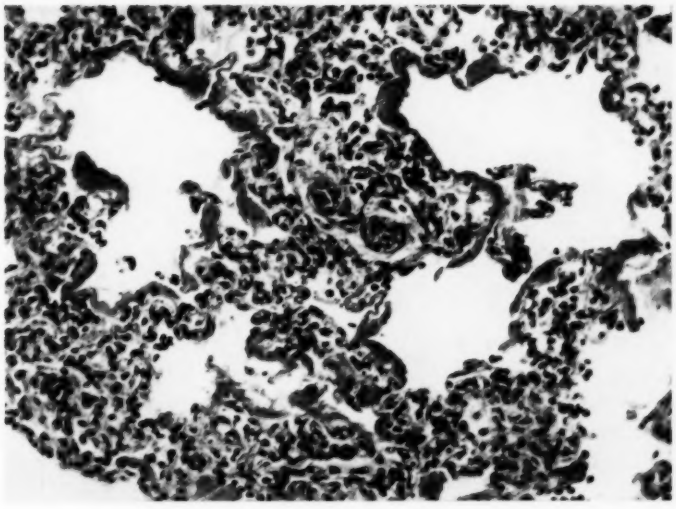


FIG. 7

Infant of diabetic mother. Lung showing resorption atelectasis with hyaline membrane formation. Haematoxylin and eosin. ×200

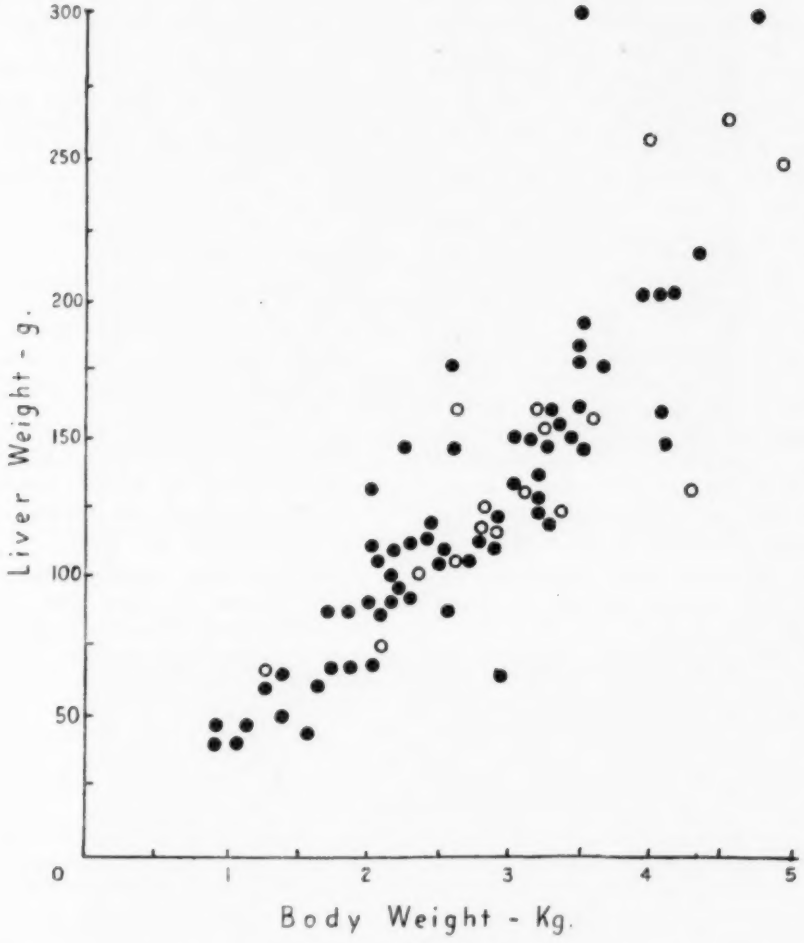



FIG. 8
Relation between liver weight and body weight in infants of diabetic (O) and non-diabetic (●) mothers.

Increased haemopoiesis has been noted by Bauer and Royster (1937), Smyth and Olney (1938), Benner (1941), Bayer (1942), Miller and Wilson (1943) in 5 out of 12 cases, White and Hunt (1943) in 14 out of 15 cases, Miller *et al.* (1944) in each of 10 cases, Miller (1945) in 2 infants of prediabetic mothers, Given *et al.* (1950) in 5 out of 13 cases, and Warren and LeCompte (1952) in all but one of 38 cases. In several instances it was considerably greater than in normal infants of similar gestational age. An increase in the number of normoblasts in the peripheral blood was noted by Miller *et al.* (1944) and Given *et al.* (1950).

An increased amount of fat was noted by Rascoff *et al.* (1938), Helwig (1940), Benner (1941), and by Given *et al.* (1950) in 6 out of 13 cases. An increase of fat and and of glycogen

was noted by Bayer (1942) and by Hultquist, Lindgren and Dalgaard (1946) in 3 cases. An increase of glycogen alone was noted by Gordon (1936) and Rössle (1942). One case (Wenig, 1941) had glycogen storage disease. Three cases have shown focal necrosis (Rössle, 1942; Given *et al.*, 1950; Potter, 1952).

The available evidence indicates that significant enlargement of the liver is uncommon and is probably due to the excessive haemopoiesis. The cause of the haemopoiesis is unknown. Potter (1952) stated that in unusually large but otherwise normal infants haemopoiesis in the liver is often increased and the blood contains more immature red cells than normal. She attributed the excessive haemopoiesis in the infants of diabetic mothers to their increased body weight. Fat and glycogen normally occur in the livers of newborn infants and sufficient information on the range of the normal amount is not yet available to assess the reports of an increase in the infants of diabetic mothers.

*Spleen.* The weights of the spleens were compared with those observed in infants of similar body weight in the control series (Fig. 11). No significant deviation from the normal range was observed.

Histological examination showed in all cases a degree of haemopoiesis slightly greater than in the control series.

White and Hunt (1943) reported that splenomegaly was almost constant and all but one of their 15 cases showed increased haemopoiesis. Warren and LeCompte (1952) concluded from a study of 45 cases that a significant enlargement was uncommon, and that any increase in weight might be accounted for by the increased erythropoiesis seen in some cases. Increased haemopoiesis has also been recorded by Bauer and Royster (1937), Miller *et al* (1944) in 3 out of 10 cases, and Miller (1945) noted it in an infant of a prediabetic mother.

### Endocrine Organs

*Pancreas.* The findings in the pancreas together with a review of the literature formed the subject of a previous paper (Cardell, 1953). In 18 infants of diabetic mothers it was found that the area of pancreatic islet tissue ranged from 1.8 to 9.9 per cent of total pancreatic tissue, compared with a normal range in newborn infants of 0.7 to 2.6 per cent. Thirteen of the 18 cases (72 per cent) showed an increase of islet tissue, which appeared to be mainly due to an increase of $\beta$ cells. There was a close correlation between the amount of islet tissue and the body weight of the infant. A further frequent and significant finding was a cellular infiltration of the pancreas composed chiefly of eosinophil leucocytes, many of which were immature.

It was concluded that an increase of islet tissue is common in the infants of diabetic mothers. An increase also occurs in the infants of prediabetic mothers and less often in erythroblastosis foetalis. Its occurrence in other infants is rare.

It was tentatively suggested that the increase of islet tissue in the infants of diabetic and of prediabetic mothers was due to over-production of the diabetogenic-growth hormone by the mother's anterior pituitary gland.

*Suprarenals.* When compared with the body weight of the infant the weight of the suprarenals in the diabetic group lay within the normal range with the exception of one case in which the weight was reduced (Fig. 12).

A histological study was made on material from 15 cases in the diabetic group and 45 cases in the control group. In addition to routine sections stained with haematoxylin and eosin, the distribution of lipoids was investigated in sections stained by mixed Sudan III and IV, by Sudan black, and in unstained sections examined by polarized light. No significant difference was found between the two groups. In the control group focal anaplasia of the foetal cortex (cytomegaly) was seen in 1 case; it was not observed in the diabetic group.

Enlargement of the suprarenals has been reported by Ringertz (1943), Miller *et al.* (1944), and Hultquist *et al.* (1946) in 3 cases. In 4 of these cases the weights are mentioned and they range from 12 to 20 g. In each case the infant weighed over 4,000 g. and these suprarenal weights are probably within the limits of the normal range (Cruickshank, Miller and Browne, 1924).

Gray and Feemster (1926) noted an increased

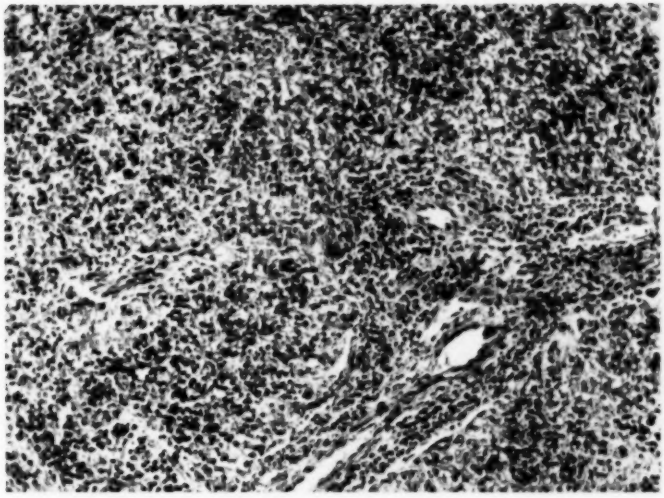


FIG. 9

Infant of diabetic mother, 35 weeks gestational age. Liver showing increased haemopoiesis. Haematoxylin and eosin. ×120

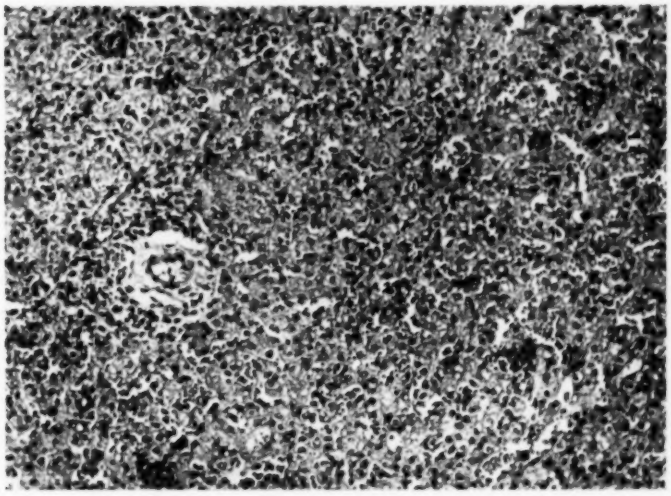


FIG. 10

Infant of non-diabetic mother, 35 weeks gestational age. Liver for comparison with Fig. 9. Haematoxylin and eosin. ×120

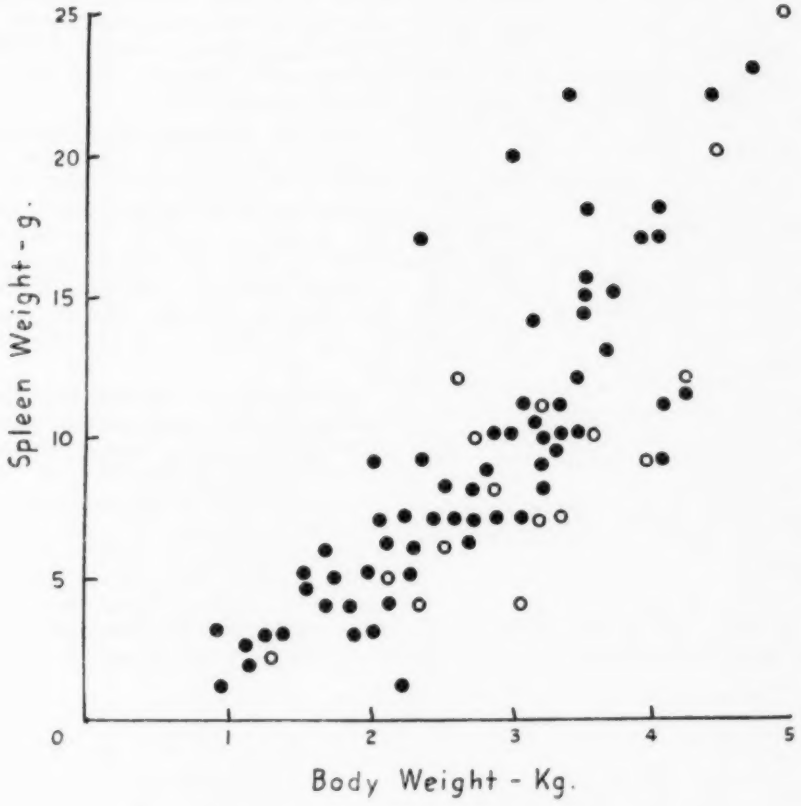



FIG. 11
Relation between spleen weight and body weight in infants of diabetic (○) and non-diabetic (●) mothers.

size of the medullary cells but, as Smyth and Olney (1938) pointed out, these were probably gangiion cells. Benner (1941) noted a case with occasional small areas of focal necrosis and polymorphonuclear cell infiltration in the cortex. Okkels and Brandstrup (1938) stated that 2 of their cases showed premature development of adrenal medullary substance. The evidence for this statement does not, however, appear in their autopsy protocols. Focal anaplasia of the foetal cortex (cytomegaly) has been reported in infants of diabetic mothers (Craig and Landing, 1951) but it has been more often reported in infants of non-diabetic mothers.

The evidence at present available suggests that there is no abnormality of the suprarenal gland in the infants of diabetic mothers.

*Thyroid.* The thyroid was examined histologically in 10 cases. Its appearance was identical with the control material examined and with the descriptions of the foetal and neonatal thyroid by Cooper (1923).

Most authors have described the thyroid as normal. The abnormalities reported are increased maturity (Okkels and Brandstrup, 1938), an increase of colloid (Smyth and Olney, 1938; Wenig, 1941), and hyperplasia (Bayer, 1942; Rössle, 1942).

*Pituitary.* The pituitary was examined histologically in 4 cases. They were identical with material examined from 8 cases in the control series and with the description of the foetal pituitary by Cooper (1923). Quite numerous eosinophil cells were seen but this is a normal feature in newborn infants.

The presence of many eosinophil cells in the anterior lobe of the pituitary has been reported by Schretter and Nevinney (1930), Bauer and Royster (1937), Okkels and Brandstrup (1938), Smyth and Olney (1938), Poursines and Cerati (1939), and Rössle (1942). Miller (1945) reported a similar finding in an infant of a prediabetic mother. Bayer (1942) doubted that a true increase of eosinophil cells occurred and stated that it was a normal feature at this age. The gland was described as normal in the cases reported by Wenig (1941), Ringertz (1943), and Warren and LeCompte (1952).

The evidence at present available indicates that there is no significant abnormality of the pituitary gland.

## Kidneys

When compared with the body weight of the infant, the weights of the kidneys in the diabetic group lay in many cases close to or below the lower limit of the normal range (Fig. 13). In view of the normal findings in other recorded series (Warren and LeCompte, 1952) this trend is probably not significant.

Potter and Thierstein (1943) concluded from a study of the kidneys of 1,000 infants that the structure of the foetal glomerulus is a valuable criterion for estimating foetal age. They stated that glomerular maturity was more closely related to foetal size than to gestational age. Immature glomeruli were found in only 5 per cent of infants weighing over 2,500 g. and in 20 per cent of infants of over 36 weeks gestational age.

In the present study the findings in the control group were in agreement with their view, but in the diabetic group many large infants were found to have immature glomeruli (Fig. 14). In infants weighing 2,500 g. or less immature glomeruli were present in 11 out of 13 cases in the diabetic group and in 2 out of 16 cases in the control group. In infants of 36 weeks or less gestational age immature glomeruli were present in 11 out of 13 cases in the diabetic group and in 15 out of 16 cases in the control group. In infants of over

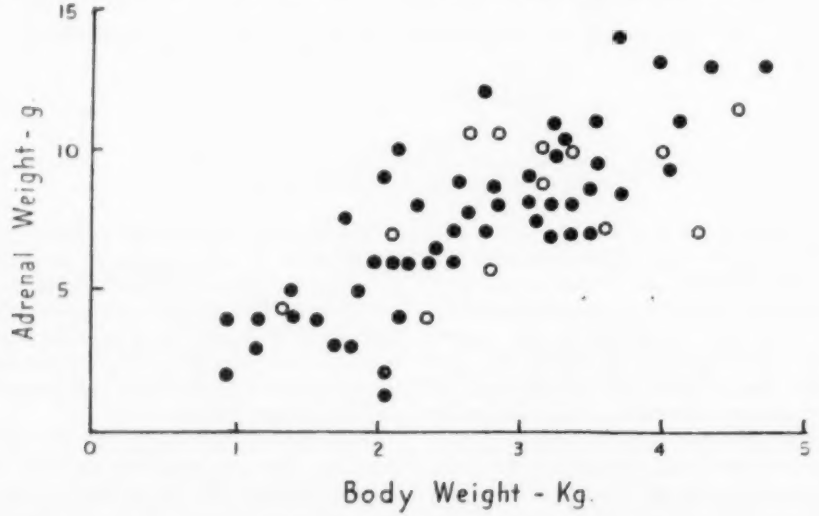



Fig. 12
Relation between adrenal weight and body weight in infants of diabetic (○) and non-diabetic (●) mothers.

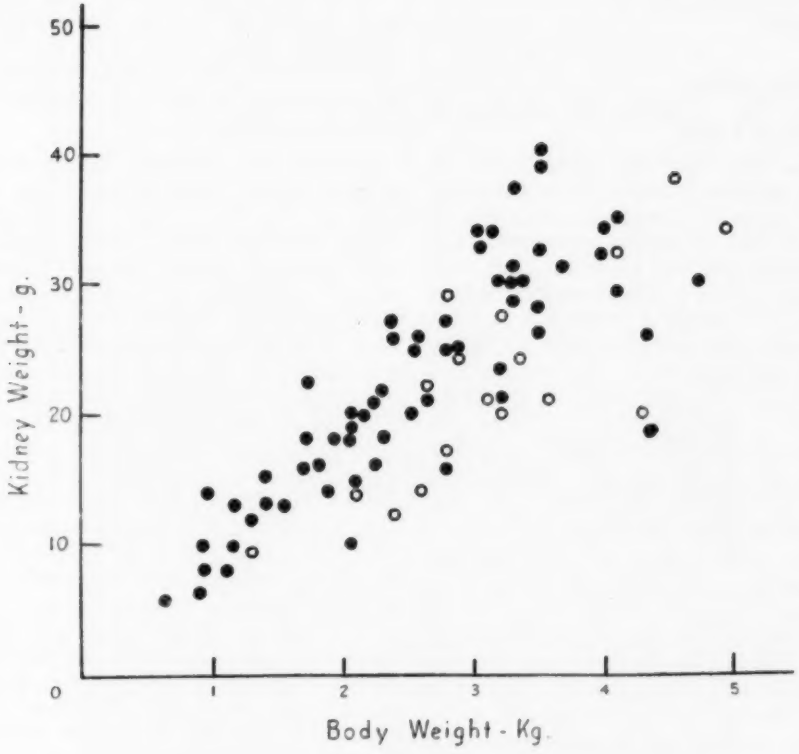



FIG. 13
Relation between kidney weight and body weight in infants of diabetic (O) and non-diabetic (●) mothers.

36 weeks gestational age immature glomeruli were present in both cases in the diabetic group and in 3 out of 19 cases in the control group.

Warren and LeCompte (1952) noted the presence of immature glomeruli in 4 infants of 34 to 36 weeks gestational age and of 3,000 to 4,200 g. body weight. They also stated that deposition of glycogen in the renal tubules may be expected when there has been an unusually high maternal blood sugar shortly before delivery, but they doubted if this was a specific finding in newborn infants. Immature glomeruli have also been noted by White and Hunt (1943) in 6 out of 15 cases, but the gestational ages and weights of these infants were not recorded.

It would appear from these findings that many of the infants of diabetic mothers, despite their large size, are premature, and that their gestational age is of greater significance in this respect than their body weight.

### GENITAL SYSTEM

*Male genital system*

The testis and prostate were examined histologically in 7 cases. The mothers of two of the infants had had hormone therapy from an early stage of pregnancy. No abnormality was noted.

Bayer (1942) considered the testis in his case to be under-developed and to show an increase of interstitial cells. Warren and LeCompte (1952) noted vacuolation of the prostatic epithelium in 2 infants whose mothers had had oestrogen

therapy. This change was not observed in the present series.

*Female genital system*

Material was available for histological examination in 4 cases.

*Case 11.* The ovary was normal showing occasional maturing follicles. The endometrium showed evidence of hyperplasia (Fig. 15). A moderate number of glands were present and many contained mucoid material. They were tortuous and lined by a tall columnar epithelium which appeared stratified in places. In some areas the inner borders of the cells were frayed. The nuclei were oval and situated in the middle of the cell with an appearance of subnuclear vacuolation.

*Case 12.* The ovary contained a moderate number of maturing follicles of up to 340 mm. diameter. The endometrium showed occasional glands lined by columnar epithelium.

*Case 13.* The mother had had hormone therapy throughout pregnancy. The ovary contained numerous large follicles of up to 1.3 mm. diameter. The theca interna was well developed, measuring 100–200$\mu$ in thickness, very vascular, and the cells were eosinophilic and lutein-like (Fig. 16). The endometrium was normal.

*Case 19.* This case was of particular interest. The mother had had hormone therapy. The uterus and oviducts were normal. The left ovary was 1.9 cm. in maximum diameter and contained several cysts of up to 1.0 cm. diameter. Sections showed many maturing follicles, some of them cystic, with a well-developed luteinized theca interna. The right gonad consisted of an elongated portion measuring 1.5 cm. resembling an ovary, and a rounded nodule 0.3 cm. in diameter situated laterally and immediately adjacent to it. Sections of the elongated portion showed ovarian tissue similar to that in the left ovary. Sections of the firm nodule showed apparently normal testicular tissue with non-canalized tubules, interstitial cells, rete testis, and epididymal tissue; no vas deferens was identified. The right gonad was therefore an ovotestis and the infant a hermaphrodite of unilateral type. No other abnormality of sexual structure was noted.

In the control material the ovaries and uterus were examined in 7 cases. One ovary showed macroscopic cysts of up to 0.2 cm. diameter. No case showed luteinization of the theca interna in the follicles and no case of endometrial hyperplasia was observed.

Schretter and Nevinney (1930) noted the presence of many follicular cysts of the ovary in their case. Smyth and Olney (1938) recorded a case in which the ovaries contained many follicular cysts and " atretic follicles ". The endometrium was thicker than normal and the glands more complicated. Benner (1941) reported a case with " stimulation of the gonads ". The ovaries contained many follicular cysts and there was well-developed luteinization of the theca interna. The endometrium showed slight desquamation of the surface epithelium, the glands were slightly branched, and red blood cells were present in the stroma. The tubal epithelium was hyperplastic and infiltrated by polymorphonuclear leucocytes. Warren and LeCompte (1952) examined the ovaries in 10 cases. Three showed follicles with theca lutein cells and in two of these cases the mothers had had hormone therapy throughout pregnancy. In a further case, in which the mother had had hormone therapy, the endometrium showed a striking decidual reaction. According to Spivack (1934) and Potter (1952) polycystic ovaries are found not uncommonly in infants of non-diabetic mothers, but luteinization of the theca interna in these cases is rare.

Warren and LeCompte (1952) tentatively suggested that the apparently increased incidence of follicular cysts with luteinization of the theca interna in infants of diabetic mothers may be due to the high concentration of chorionic gonadotrophin which occurs in diabetic pregnancies (White, 1952) or to an excess of insulin from the hyperplastic pancreatic islets of these infants. They quote the work of Abel (1931) who observed follicular development and formation of many corpora lutea in adult female mice given large doses of insulin.

In the present series the 2 cases with cystic follicles and luteinization of the theca interna had pancreatic islet areas of 5.5 and 6.9 per cent respectively (normal range, 0.7 to 2.6 per cent),

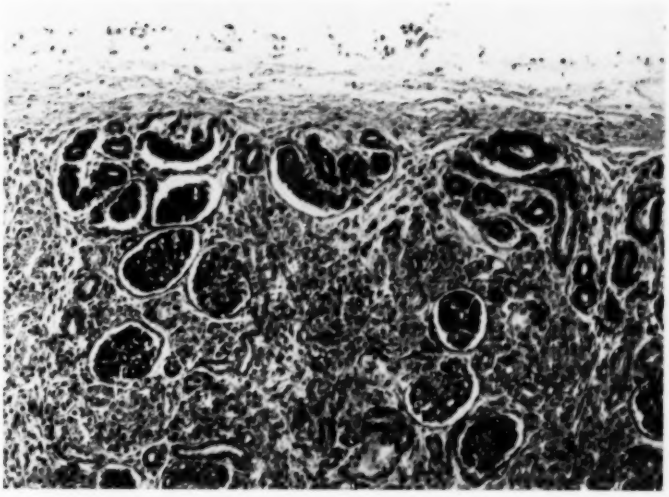


FIG. 14

Infant of diabetic mother, 36 weeks gestational age, weighing 4,540 g. Kidney showing immature glomeruli. Haematoxylin and eosin. ×120.

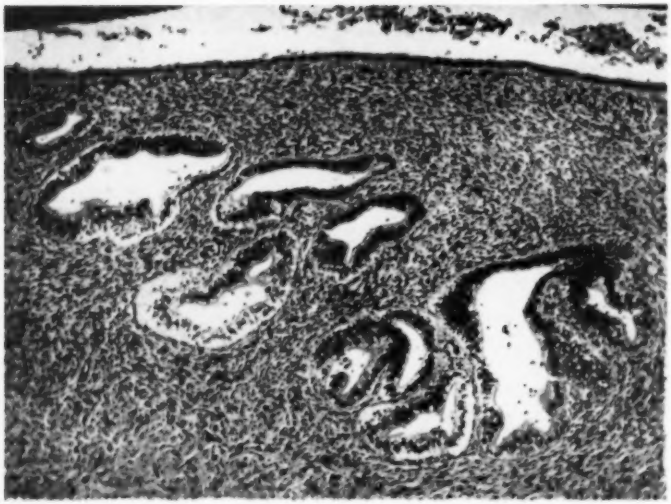


FIG. 15

Infant of diabetic mother. Endometrium showing hyperplastic glands. Haematoxylin and eosin. ×70

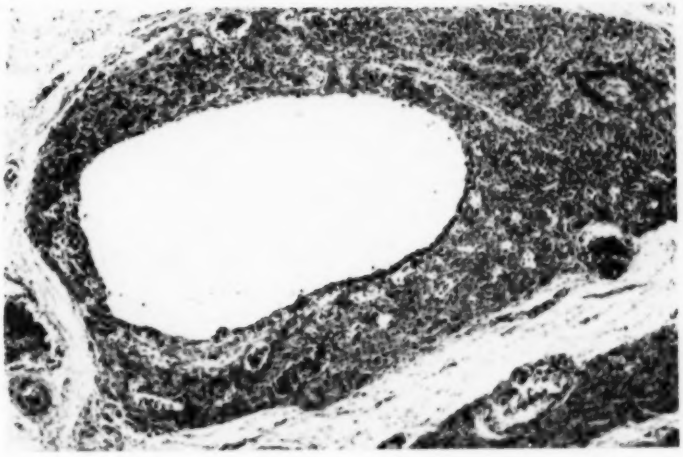


FIG. 16

Infant of diabetic mother. Ovary showing follicular cyst with luteinization of the theca interna. Haematoxylin and eosin. × 70

and both mothers had had hormone therapy. The 2 cases without these ovarian lesions had pancreatic islet areas of 1.8 and 3.7 per cent and the mothers did not have hormone therapy. Further investigation will be necessary to assess the significance of these observations.

The finding of hyperplastic changes in the endometrium in one case in the present series is probably not significant. Similar changes were noted by Spivack (1934) in 5 out of a series of 23 newborn infants.

*Effects of maternal hormone therapy on foetal genital system*

The possible effect of hormones acting *in utero* on the development of the genital system are not yet fully known. The results of experimental work are discordant (Greene, 1944; Moore, 1947). Davis and Potter (1948) found no changes in the sex organs of foetuses obtained by therapeutic abortion in a series of women receiving stilboestrol therapy.

The current extensive use of hormone therapy (stilboestrol and ethisterone) in pregnant diabetic women would seem to warrant further experimental work in view of the lesions found in some of the infants of these women. In the present series together with that of Warren and LeCompte (1952) the following lesions have been noted: ovaries with many follicular cysts and luteinization of the theca interna, 4 cases; ovotestis, 1 case; decidual reaction in endometrium, 1 case; and vacuolation of prostatic epithelium, 2 cases.

## Bones

The centres of ossification were examined in 13 cases. Some evidence of advanced bone age was seen in 2 cases, an infant of 34 weeks gestational age with a centre of ossification present in the distal femoral epiphysis and an infant of 36 weeks gestational age with a centre of ossification present in the proximal tibial epiphysis. One case showed a retarded bone age, an infant of 36 weeks gestational age not showing a centre of ossification in the distal femoral epiphysis. No histological studies were made.

These results suggest that there is little, if any, deviation from normal in ossification in the infants of diabetic mothers.

Warren and LeCompte (1952) in a histological study found no difference between their diabetic and control series.

## Placenta

The placenta was examined in 12 cases. In several instances it appeared to be bulky. The weight ranged from 18 to 30 per cent of the infant's weight. Histological examination showed no significant deviation from normal placentas. In one case there was a mild chorionitis. These findings suggest that the placenta is essentially normal. A further study on placentas from all diabetic pregnancies is now in progress.

Reis, DeCosta and Allweiss (1950) examined the placenta in 10 cases and reported that the changes found did not vary either qualitatively or quantitatively from those found in placentas of non-diabetic patients. Warren and LeCompte (1952) examined 54 diabetic placentas. The only abnormality noted was an increase in weight. The figures they obtained were 195.5 g. per kg. baby weight in diabetics as opposed to 165.5 g. for a control group. McKay (1952) reported on 28 placentas of diabetic mothers who had all had hormone therapy. There was stromal oedema of the larger villi which had the appearance of immature villi. The cytotrophoblastic cells of the Langhans layer were prominent and many showed mitotic figures.

In view of the current theory that attributes the maternal sex-hormone imbalance and the high intra-uterine death rate to placental degeneration, the changes hitherto recorded in the placenta are disappointing. Further histochemical studies are urgently required.

## Congenital Abnormalities

The figures given below for the incidence of congenital abnormalities in the infants of both diabetic and non-diabetic mothers relate to autopsies performed between April 1947 and September 1952 on infants who were stillborn or who died within 48 hours of birth. Congenital abnormalities were present in 6 out of 24 cases (25 per cent) in the diabetic group and in 20 out of 99 cases (20.2 per cent) in the control group. The incidence figures in the two groups are not significantly different.

The abnormalities found in the diabetic group were: bilateral hydronephrosis and hydro-ureter with a valve in the prostatic urethra, double ureter and renal pelvis, obliteration of one ureter, supernumerary pulmonary valve cusp, ovotestis and ectopic adrenal cortical tissue. In none of these cases could the abnormality be considered to play any part in the death of the infant.

The majority of authors have reported an increase of congenital abnormalities in the infants of diabetic mothers. White (1952) noted an incidence of 80 per cent compared with an expected incidence of 1.8 per cent.* Congenital abnormalities were stated to account for 14 per cent of foetal deaths. She considered them to be of genetic origin in view of similar anomalies occurring in diabetics. Peel and Oakley (1950) found an incidence of 6.3 per cent compared with 0.94 per cent in their control series. Warren and LeCompte (1952), in an autopsy study of 50 cases, found 9 to have congenital abnormalities, and in 3 cases the defects were considered to be the cause of death. Miller (1946) found 6 cases with congenital abnormalities in a series of 19 autopsies. These last two series do not quote an incidence figure for autopsy material in infants of non-diabetic mothers.

There are, however, many reports in which no increase has been observed: Potter and Adair (1938), Mengert, Laughlin and Kuder (1939), Bill and Posey (1944), Patterson and Burnstein (1949), Reis *et al.* (1950), Hall and Tillman (1951), and Moss and Mulholland (1951).

In conclusion one can only state that the evidence for the increased incidence of congenital abnormalities in infants of diabetic mothers is still unsatisfactory.

## Cause of Death

No foetal cause for death was discovered in the 6 stillborn cases in the present series. Of the 19 liveborn infants, 1 died at the age of 3 weeks from gastro-enteritis. The remainder died within 24 hours of birth. Eleven showed resorption atelectasis with hyaline membrane formation, and in 5 the cause of death was recorded as "atelectasis" but no histological study was performed. One died of paroxysmal ventricular tachycardia with cardiac hypertrophy, and the remaining case died of bronchopneumonia.

Warren and LeCompte (1952) listed the causes of death in their 50 cases as follows: undetermined (including 11 macerated stillbirths), 18; prematurity (under 32 weeks or 1,500 g.), 13; atelectasis with hyaline membrane, 8; birth injury, 4; pneumonia, 3; congenital abnormality, 3; and adrenal haemorrhage, 1. They concluded that the reasons for the high intra-uterine and neonatal death rate remained obscure.

However, in the liveborn cases, with the possible exception of an increased incidence of lethal congenital abnormalities, the causes of death are the same as those found in infants of non-diabetic mothers. It is now generally accepted that hypoglycaemia is rarely, if ever, responsible for death. The frequent finding in these infants of resorption atelectasis with hyaline membrane formation serves to emphasize that they are often premature infants despite their large size. It would seem, therefore, that in these infants there is some factor or group of factors responsible both for the increased susceptibility of the liveborn to the normal hazards of early neonatal life and for the high intra-uterine death rate.

## Experimental

Experimental studies have so far failed to shed much light on the problem of foetal mortality in diabetic pregnancy. Pregnant alloxan diabetic animals of various species show a high incidence of intra-uterine foetal deaths (Davis, Fugo and Lawrence, 1947; Miller, 1947; Barns *et al.*, 1950). Pregnant pancreatectomized diabetic animals react in a similar manner and, in addition, in some cases the foetus is overweight and shows some internal changes resembling those found in human infants (Gordon, 1936; Hultquist, 1950).

The administration of various hormones, particularly anterior pituitary growth hormone, to pregnant rats has resulted in a high foetal mortality and, in some cases, the production of over weight foetuses (Hultquist and Engfeldt, 1949; Barns *et al.*, 1950; Barns and Swyer, 1952). Chorionic gonadotrophin and thyrotrophic

* The figure 80 per cent appears to be a misprint; 12 per cent is the figure given in her 1946 paper.

hormone have produced similar but less definite results.

## Discussion

The pregnancies of diabetic and prediabetic women are characterized by a high foetal mortality and by a number of abnormal features in the infants. The factors responsible for these occurrences are unknown. The subject has been extensively discussed by Eastman (1946), Peel and Oakley (1950), and Bachman (1952). The current hypothesis is that over-activity of the maternal anterior pituitary gland is responsible for foetal changes and also produces degenerative changes in the placenta which result in toxaemia and intra-uterine foetal death. The abnormalities in excretion of gonadotrophin, oestrogen, and pregnanediol in the mother are considered to result from impaired placental function. This view is attractive but is not yet supported by adequate evidence.

That maternal factors may not be the only ones has recently been shown by Jackson (1952). He found that the infants of prediabetic fathers are overweight, but to a lesser degree than those of prediabetic mothers. There was no increase of foetal mortality in these cases. He concluded that the size of the infants of prediabetic mothers was in part due to an inherited factor and in part due to the maternal environment. It is not impossible that some of the other features of these infants are due to a hereditary factor. If one may speculate for a moment, the finding of pancreatic islet lesions in infants of diabetic fathers like those found in infants of diabetic mothers might be of significance in relation to the hereditary factor in diabetes mellitus.

Miller *et al.* (1944) have stressed the similarity between the infants of diabetic mothers and infants with erythroblastosis foetalis. These similarities (enlargement of heart, liver, and spleen; increase of pancreatic islet tissue and of haemopoiesis) are more apparent than real. In the infants of diabetic mothers enlargement of the liver and spleen is rare, the increase of pancreatic islet tissue is of much greater frequency and degree, and the haemopoiesis is not associated with evidence of haemolysis.

The only definite conclusion that can be drawn from this study is that further investigation is required. It is hoped that these observations may help to stimulate interest in the pathology of these infants, a subject much neglected in this country.

## Summary

The abnormal findings at postmortem in 25 infants of diabetic mothers are reported and compared with those recorded in the literature.

As a group these infants show certain characteristic features:

(1) *Macrosomia.* They are larger than normal and the increase in weight parallels the increase in length. Bone structure and ossification are normal. There is some evidence to suggest that the increase in size occurs in the later part of intra-uterine life. Despite their large size many of these infants are premature.

(2) *Visceromegaly.* With a few exceptions organ weight is proportional to body weight. In a small number of cases there is significant cardiac enlargement, due in part only to an increase of muscle glycogen. In most cases the brain is small.

(3) *Haemopoiesis.* The liver and spleen frequently show an increased degree of haemopoiesis. There is no increased haemosiderosis.

(4) *Endocrine glands.* The pancreas frequently shows an infiltration by eosinophils and an increase of islet tissue due to an increase of $\beta$ cells. There is a significant correlation between the amount of pancreatic islet tissue and body weight. The adrenal, pituitary, and thyroid glands show no abnormality.

(5) *Kidneys.* Immature glomeruli are frequently found, supporting the contention that despite their large size many of these infants are premature.

(6) *Genitalia.* There appears to be a significant increase in the incidence of follicular ovarian cysts with luteinization of the theca interna. In the infants of mothers receiving hormone therapy there are occasional reports of genital abnormalities.

(7) *Placenta.* Apart from an increase of size no significant lesions have yet been described.

(8) *Congenital abnormalities.* There is some evidence to suggest that there is an increased

incidence of congenital abnormalities. It was not noted in the present series.

(9) *Cause of death.* Resorption atelectasis with hyaline membrane formation is a common finding in the liveborn infants.

The reason for the high foetal mortality and the abnormalities in the infants of diabetic mothers is unknown. Over-activity of the maternal anterior pituitary gland is an attractive theory but it is not yet supported by adequate evidence. It is possible that genetic factors may play some part.

I wish to thank Professor H. A. Magnus for his help and advice throughout this investigation, and Mr. J. H. Peel and Mr. S. G. Clayton for their interest and for access to the case records. I am indebted to Mr. G. Harwood for the histological preparations and to Mr. W. Smith for the photomicrographs.

## References

Abel, P. (1931): *Arch. Gynäk.*, **147**, 444.
Bachman, C. (1952): *Amer. J. med. Sci.*, **223**, 681.
Barns, H. H. F., Lindan, O., Morgans, M. E., Reid, E., and Swyer, G. I. M. (1950): *Lancet*, **2**, 841.
Barns, H. H. F., and Swyer, G. I. M. (1952): *Brit. med. J.*, **2**, 914.
Bauer, J. T., and Royster, H. A., jr. (1937): *Bull. Ayer clin. Lab.*, **3**, 109.
Bayer, J. (1942): *Virchows Arch.*, **308**, 659.
Benner, M. C. (1941): *Arch. Path.*, **32**, 818.
Bill, A. H., and Posey, F. M., jr. (1944): *Amer. J. Obstet. Gynec.*, **48**, 405.
Blystad, W., Landing, B. H., and Smith, C. A. (1951): *Pediatrics*, **8**, 5.
Bruns, P. D., and Shields, L. V. (1951): *Amer. J. Obstet. Gynec.*, **61**, 953.
Cardell, B. S. (1953): *J. Path. Bact.*, **66**, 335.
Cooper, E. R. A. (1923): *The histology of the more important human endocrine organs at various ages.* Oxford University Press, London.
Craig, J. M., and Landing, B. H. (1951): *Amer. J. Path.*, **27**, 721.
Cruickshank, J. N., Miller, M. J., and Browne, F. J. (1924): *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 86.
Davis, M. E., Fugo, N. W., and Lawrence, K. G. (1947): *Proc. Soc. exp. Biol., N.Y.*, **66**, 638.
Davis, M. E., and Potter, E. L. (1948): *Endocrinology*, **42**, 370.
Dubreuil, G., and Anderodias, J. (1920): *C. R. Soc. Biol. Paris*, **83**, 1490.
Eastman, N. J. (1946): *Obstet. Gynec. Surv.*, **1**, 3.
Given, W. P., Douglas, R. G., and Tolstoi, E. (1950): *Amer. J. Obstet. Gynec.*, **59**, 729.
Gordon, W. H. (1936): *Ohio St. med. J.*, **32**, 540.
Gray, S. H., and Feemster, L. C. (1926): *Arch. Path.* **1**, 348.
Greene, R. R. (1944): *J. clin. Endocrinol.*, **4**, 335.
Hall, R. E., and Tillman, A. J. B. (1951): *Amer. J. Obstet. Gynec.*, **61**, 1107.
Helwig, E. B. (1940): *Arch. intern. Med.*, **65**, 221.
Hultquist, G. T. (1950): *Acta. path. microbiol. scand.*, **27**, 695.
Hultquist, G. T., and Engfeldt, B. (1949): *Acta endocrinol.*, **3**, 365.
Hultquist, G. T., Lindgren, I., and Dalgaard, J. B (1946): *Nord. Med.*, **31**, 1841.
Hurwitz, D., and Irving, F. C. (1937): *Amer. J. med. Sci.*, **184**, 85.
Jackson, W. P. U. (1952): *Brit. med. J.*, **2**, 690.
Macklin, M. T. (1944): *J. Pediat.*, **25**, 533.
McKay, D. G. (1952), cited by White (1952).
Mengert, W. E., Laughlin, K., and Kuder, K. (1939): *Surg. Gynec. Obstet.*, **69**, 615.
Miller, H. C. (1944): *Yale J. Biol. Med.*, **16**, 509.
Miller, H. C. (1945): *Amer. J. med. Sci.*, **209**, 407.
Miller, H. C. (1946): *J. Pediat.*, **29**, 455.
Miller, H. C. (1947): *Endocrinology*, **40**, 251.
Miller, H. C., Johnson, R. D., and Durlacher, S. H. (1944): *J. Pediat.*, **24**, 603.
Miller, H. C., and Wilson, H. M. (1943): *J. Pediat.*, **23**, 251.
Moore, C. R. (1947): *Embryonic sex hormones and sexual differentiation.* Thomas, Springfield, Ill.
Moss, J. M., and Mulholland, H. B. (1951): *Ann., intern. Med.* **34**, 678.
Okkels, H., and Brandstrup, E. (1938): *Acta path. microbiol. scand.*, **15**, 268.
Patterson, M., and Burnstein, N. (1949): *Arch. intern. Med.*, **83**, 390.
Peel, J., and Oakley, W. (1950): *Trans. 12th Brit. Congr. Obstet. Gynaec.*, p. 161.
Potter, E. L. (1952): *Pathology of the fetus and the newborn.* Year Book Publishers, Chicago.
Potter, E. L. and Adair, F. L. (1938): *Amer. J. Obstet. Gynec.*, **35**, 256.
Potter, E. L., and Adair, F. L. (1949): *Fetal and neonatal death.* 2nd edition. University of Chicago Press, Chicago.
Potter, E. L., and Thierstein, S. T. (1943): *J. Pediat.*, **22**, 695.
Poursines, Y., and Cerati, P. (1939): *Ann. Anat. path.*, **16**, 673.
Rascoff, H., Beilly, J. S., and Jacobi, M. (1938): *Amer. J. Dis. Child.* **55**, 330.
Reis, R. A., DeCosta, E. J., and Allweiss, M. D. (1950): *Amer. J. Obstet. Gynec.*, **60**, 1023.
Ringertz, N. (1943): *Nord. Med.*, **19**, 1302.
Rössle, R. (1942): *Virchows. Arch.*, **308**, 676.

Schretter, G., and Nevinney, H. (1930): *Arch. Gynäk.*, **143**, 465.

Smyth, F. S., and Olney, M. B. (1938): *J. Pediat.*, **13**, 772.

Spivack, M. (1934): *Amer. J. Obstet. Gynec.*, **27**, 157.

Warren, S., and LeCompte, P. M. (1952): *The pathology of diabetes mellitus.* 3rd edition. Kimpton, London.

Wenig, K. (1941): *Frankfurt. Z. Path.*, **55**, 118.

White, P. (1946), *in* Joslin, E. P., Root, H. F., White, P., Marble, A., and Bailey, C. C.: *Treatment of diabetes mellitus.* 8th edition. Kimpton, London.

White, P. (1952), *in* Joslin, E. P., Root, H. F., White, P., and Marble, A.: *Treatment of diabetes mellitus.* 9th edition. Kimpton, London.

White, P., and Hunt, H. (1943): *J. clin. Endocrinol.*, **3**, 500.

# THE POSITION OF THE FOETUS IN RELATION TO PLACENTAL SITE*

BY

A. S. WHITEHEAD, M.D., M.Rad., D.M.R.D.

*Consulting Radiologist*

*Mill Road Maternity Hospital, Liverpool*

## INTRODUCTION

IT has long been recognized that when the placenta is praevia malpresentation is common, but it is only in recent years that it has been suggested by Stevenson (1949, 1950, 1951) that even when the placenta is in the upper uterine segment its particular site may influence the lie and presentation of the foetus in late pregnancy and labour. This suggestion arose from the results of a study of cases by means of soft tissue radiography. The work reported here was undertaken in an attempt to confirm or refute Stevenson's findings.

## MATERIAL

During the period January 1949 to September 1952 soft tissue placentography was carried out on 500 women at Mill Road Maternity Hospital, Liverpool, and by this means the position of the placenta was diagnosed in each one. The actual site of the placenta was subsequently confirmed, either at the time of Caesarean section or by intra-uterine palpation at the conclusion of the second stage of labour, in 150 of these cases without any error in prediction of the placental site being revealed. Although the accuracy of the radiological assessment was not actually confirmed in the remaining 350 cases, their subsequent clinical course did not suggest that any error in diagnosis had been made. The cases were not unselected for many women were referred for examination because of antepartum haemorrhage or other clinical feature which raised the question of placenta praevia. The series is therefore loaded with a high proportion of cases of low insertion of the placenta and this is seen especially in the group in which the foetus presented by the head. The cases of breech presentation and transverse lie were unselected, all examples of these conditions being referred to the X-ray department by special arrangement.

Only those women X-rayed at or after the 34th week are included. When there was reason to question the duration of amenorrhoea, foetal maturity at the time of examination was assessed retrospectively from the estimated maturity of the child at birth.

The technique of soft tissue placentography employed is based on that devised by Snow and Powell (1934) and subsequently modified by Vaughan, Weaver and Adamson (1942). It is described in detail elsewhere (Whitehead, 1953).

## RESULTS

Despite the disadvantages of partial selection the series does lend itself to examination in respect of certain problems connected with the relative positions of the foetus and the placenta.

### (1) *The relative frequency of different placental sites*

It is well established that, no matter whether the placental site be in the upper or lower segment of the uterus, it is usually on the anterior or posterior wall and rarely on the lateral. This is confirmed by the findings shown in Table I as well as those of the more recent of those observers whose conclusions are set out in Table II. In Table I a "fundal" site means that the placenta was situated more or less symmetrically in the fundus, whereas "cornual" denotes an asymmetrical implantation—over one or other cornu of the uterus.

* This paper in an abbreviated form was presented to a meeting of the Gynaecological Visiting Society of Great Britain, held in Liverpool, October 1952.

TABLE I

| Presentation | Head | Breech | Transverse and oblique lies | Total |
|---|---|---|---|---|
| Total cases ... ... ... ... | 262 | 187 | 51 | 500 |
| Normal anterior placenta ... ... | 112 | 43 | 22 | 177 |
| Normal posterior placenta ... ... | 113 | 27 | 6 | 146 |
| Antero-lateral placenta ... ... | 2 | 3 | 1 | 6 |
| Lateral placenta ... ... ... | 4 | 1 | 0 | 5 |
| Fundal placenta ... ... ... ... | 2 | 20 | 10 | 32 |
| Cornual placenta ... ... ... | 4 | 90 | 0 | 94 |
| Anterior placenta praevia ... ... | 8 | 2 | 7 | 17 |
| Posterior placenta praevia ... ... | 17 | 1 | 5 | 23 |

TABLE II

*Frequency of the various placental sites*
(Upper uterine segment insertions only)

| Author | Total | Ant. Per cent | Post. Per cent | Lat. Per cent | Fundal and Cornual Per cent |
|---|---|---|---|---|---|
| Holzapfel* (1896) ... ... ... | 107 | 35.5 | 33.6 | 23.4 | 6.6 |
| Gusserow* (1866) ... ... ... | 100 | 41 | 37 | 13 | 9 |
| Dippel and Brown (1940) ... ... | 236 | 43 | 45 | – | – |
| Torpin and Holmes (1943) ... ... | 363 | 45 | 55 | – | – |
| Reid (1951) ... ... ... ... | 487 | 44 | 46 | – | 3 |
| Stevenson (1949) ... ... ... | 474 | 43.8 | 31.6 | 9.7 | 7.4 |
| Whitehead ... ... ... ... | 500 | 35.4 | 29.2 | 2.2 | 25.2 |

* These writers assessed placental site by clinical methods only, the others used soft tissue placentography.

As indicated previously the number of cases of placenta praevia in head presentation (Table I) does not reflect the true incidence of the condition—it is inflated by selection of women suffering from antepartum haemorrhage. Moreover, the deliberate selection of all cases of breech presentation and transverse lie for X-ray investigation unbalances the whole series, and results in a far greater number of fundal and cornual insertions than would ordinarily be found in an unselected series of consecutive cases of pregnancy.

Examples of anterior, posterior, lateral, fundal and cornual implantations of the placenta are shown in Figures 1, 2, 3, 4, 5.

(2) *Does the foetus face the placenta?*

The old statement, based mainly on clinical impressions, that the foetus usually faces the placenta, its ventral surface being nearest to the foetal aspect of the placenta, was not refuted by the earlier studies in soft tissue radiography of Snow and Rosensohn (1939), Buxton, Hunt and Potter (1942), Smith (1943), Torpin and Holmes (1943), and Bishop (1945). Dippel and Brown (1940) were the first to declare that the foetus does not usually face the placenta, and their findings have been confirmed in the present series (Table III).

TABLE III

*Relationship of foetus to placenta (percentage figures)*

| | Placenta anterior (150 cases) | Placenta posterior (131 cases) |
|---|---|---|
| Foetus facing placenta ... | 21 | 37 |
| Foetal back to placenta ... | 20 | 13 |
| Foetal side to placenta ... | 58 | 50 |
| Foetus unstable ... ... | 1 | – |

Table III suggests that when the placenta is anterior the foetus is just as likely to have its back as its face to it; when the placenta is posterior the foetus may face it more frequently. In fact, however, in the majority of cases the

foetus lies with one or other of its sides directed to the placenta. This is as might be expected in view of the known frequency of the lateral position of the occiput. In a recent series of 158 consecutive primigravidae with known normal pelves, X-rayed at or near term, the relative frequency of foetal positions was as shown in Table IV.

TABLE IV
*Frequency of the various positions of the occiput*

| Position | Percentage |
|---|---|
| Occiput lateral ... ... ... ... | 54 |
| Occiput obliquely anterior ... ... ... | 30 |
| Occiput directly anterior ... ... ... | 8 |
| Occiput obliquely posterior ... ... | 5 |
| Occiput directly posterior ... ... ... | 3 |

(3) *The placental site in cases of transverse and oblique lie*

The position of the placenta was determined in 51 cases in which a transverse or oblique lie was present at or after the 34th week, and the findings are shown in Table V. In 20 cases the abnormal lie persisted until term; 17 of these were treated by Caesarean section and 3 by external version during early labour followed by vaginal delivery. In the remaining 31 cases spontaneous version occurred during late pregnancy or early labour, 29 of the foetuses ultimately presenting by the head and 2 by the breech.

TABLE V
*Placental site in transverse and oblique lie*

| Placental Site | Number |
|---|---|
| Anterior ... ... ... ... ... | 22 |
| Posterior ... ... ... ... | 6 |
| Antero-lateral ... ... ... ... | 1 |
| Lateral ... ... ... ... ... | 0 |
| Fundal ... ... ... ... ... | 10 |
| Cornual ... ... ... ... ... | 0 |
| Anterior praevia ... ... ... | 7 |
| Posterior praevia ... ... ... | 5 |
| Total ... ... ... ... ... ... | 51 |

Table V shows that, when the foetus lies transversely, the placenta is most often found on the anterior wall of the upper segment but that fundal and praevia implantations are relatively common. Posterior implantation, however, is rare. These findings are in general agreement with those of Stevenson (1949), who argued that implantation of the placenta in either pole of the uterus (fundus or lower segment) tends to displace the foetus from a longitudinal lie by shortening the available long axis of the uterine cavity. This mechanism, he maintained, is favoured by an associated laxity of the uterine and abdominal musculature, and the high parity of many of his patients was quoted to support this argument. He also postulated that, although anterior implantation of the placenta might permit transverse lie, especially if the uterus is lax, posterior implantation is not conducive to it because the placenta in such a position tends to "splint" the longitudinal lie. Although the findings in this respect are not quite as clear cut as postulated by Stevenson, they nevertheless suggest that his arguments are in part valid—and this is especially true bearing in mind that the placental site is only one of many possible factors which may influence the lie of the foetus. There is certainly a significant difference in the distribution of placental sites as between series of longitudinal and transverse lies.

(4) *The placental site in breech presentation*

Table VI shows the radiological findings in the 187 consecutive cases in which the breech was presenting at or after the 34th week of pregnancy. The subsequent history and mode of delivery in these cases is shown in Table VII.

TABLE VI
*Distribution of the placental site in breech presentations*

| Placental site | Type of breech presentation: Extended legs | Flexed legs | One leg flexed, one extended | Total |
|---|---|---|---|---|
| Anterior | 25 | 9 | 9 | 43 |
| Posterior | 20 | 2 | 5 | 27 |
| Antero-lateral | 1 | 0 | 2 | 3 |
| Lateral | 0 | 1 | 0 | 1 |
| Fundal | 9 | 9 | 2 | 20 |
| Cornual | 58 | 21 | 11 | 90 |
| Anterior praevia | 0 | 1 | 1 | 2 |
| Posterior praevia | 1 | 0 | 0 | 1 |
| Total | 114 | 43 | 30 | 187 |

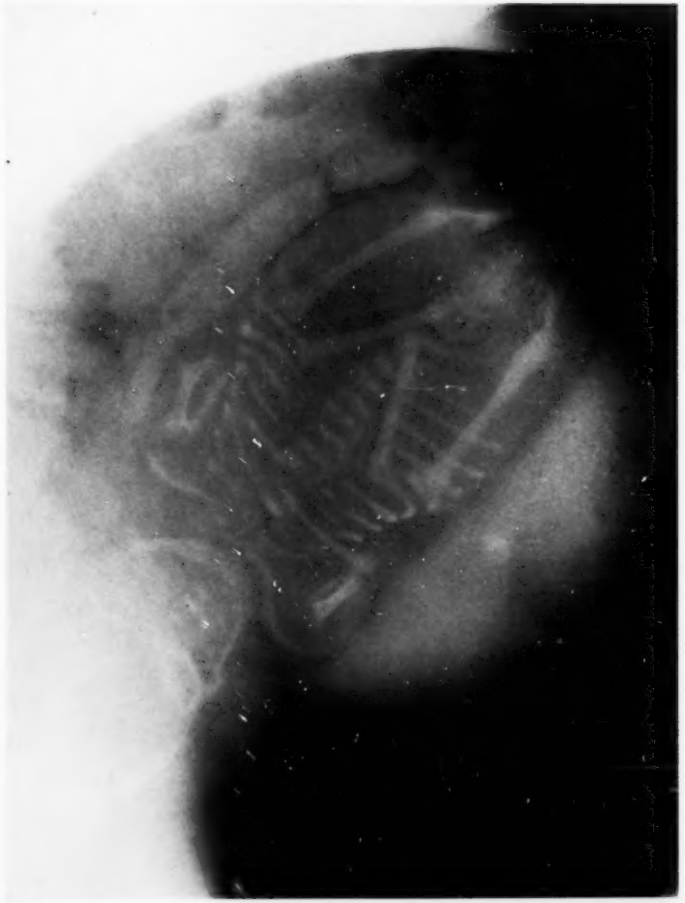


FIG. 1

Lateral view showing placenta on the anterior wall of the upper uterine segment

FIG. 2

Lateral view of an anterior placenta praevia, the lower part of it obscured by the maternal pelvic bones. Forward displacement of the foetal head with over-riding of the symphysis pubis is also well shown.

A.S.W.

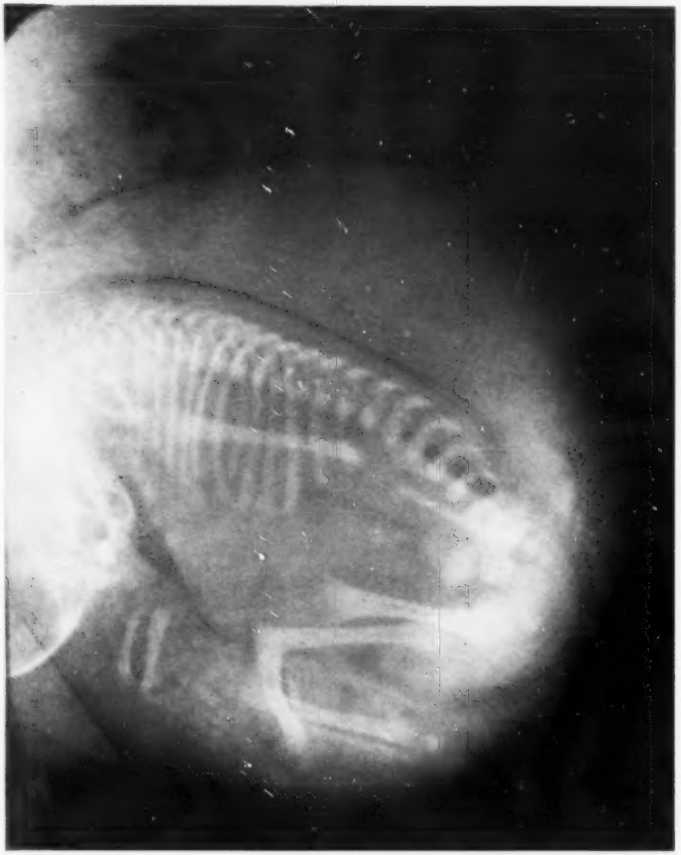


FIG. 3

Lateral view showing placenta on the posterior wall of the upper segment of a pendulous uterus.

FIG. 4

Lateral view showing the lower part of a posterior placenta praevia.

FIG. 5

Anterior-posterior view of a " cornual " placenta, the foetus presenting by the breech.

FIG. 6

Lateral view of a placenta situated mainly in the fundus of the uterus, the foetus lying transversely.

TABLE VII

| | |
|---|---|
| Spontaneous cephalic version and vaginal delivery | 76 cases |
| External cephalic version and vaginal delivery | 17 cases |
| Breech delivery with or without previous attempts at version | 77 cases |
| Caesarean section | 9 cases |
| Subsequent history not known | 8 cases |
| Total | 187 cases |

It is of considerable interest to compare the ultimate outcome of each of the cases of breech presentation with the position of the placenta. Table VIII contrasts the placental site with the subsequent mode of delivery in those cases in which the subsequent clinical history is available.

The most striking result of the analysis of the over-all figures for breech presentation (Table VI) is the high proportion of cornual implantations—almost 50 per cent as compared with less than 2 per cent in cephalic presentation. The findings in this respect, moreover, become even more convincing when only cases of *persistent* breech presentation are analyzed (Table VIII). Indeed, the figures here strongly suggest that persistent breech presentation is much more likely to occur when the placenta covers a cornu of the uterus, thus confirming the findings of Stevenson (1950, 1951). They do not mean, however, that a persistent breech presentation can only occur when the placenta is situated over one cornu. It would be unreasonable to expect this for other factors such as the attitude of the foetus and abnormalities in uterine shape also play a part. Nevertheless, it would appear that spontaneous version is unlikely to occur when the placenta is cornual, whereas it is relatively common when the placenta is situated on either the anterior or posterior wall of the uterus.

Stevenson (1950, 1951) related the association between breech presentation and implantation of the placenta over a cornu of the uterus to the effect of such an arrangement on the shape of the available uterine cavity. He argued that a cornual placenta narrows the upper pole of the uterus to a size similar to that of the lower pole and the foetal breech is then just as easily accommodated in one as in the other. The investigation reported here gives no information which allows comment on the validity of this explanation of the unquestionable relation between cornual implantation of the placenta and breech presentation.

It is of interest to note that in not one of the 262 cases of head presentation did spontaneous version to breech presentation occur in the later weeks of pregnancy.

## SUMMARY

(1) The position of the placenta in 500 women at or after the 34th week of pregnancy was determined by soft tissue placentography and related to the position of the foetus.

(2) When the foetal head presents the placenta is usually implanted on the anterior or posterior wall of the upper uterine segment of the uterus. The fundus and lateral walls are much less often the site of implantation.

(3) In cases of transverse or oblique lie the placenta is most frequently situated in the fundus, in the lower uterine segment, or on the anterior wall of the upper uterine segment. It

TABLE VIII

*Comparison between mode of delivery and placental site in breech presentation*

| Mode of delivery | Placental site | | | | | |
|---|---|---|---|---|---|---|
| | Cornual | Fundal | Ant. | Post. | Lat. | Praevia |
| Assisted breech delivery | 56 | 5 | 12 | 3 | 1 | – |
| Caesarean section | 4 | 1 | – | 1 | – | 3 |
| Spontaneous cephalic version and vaginal delivery | 15 | 11 | 29 | 21 | – | – |
| External cephalic version and vaginal delivery | 12 | 3 | 1 | 1 | – | – |
| Total | 87 | 20 | 42 | 26 | 1 | 3 |

is rarely found on the posterior wall of the upper uterine segment.

(4) When the breech presents there is a significant difference in various placenta implantations. The placenta is more often found to cover one cornu of the uterus.

(5) Cornual implantation of the placenta appears to favour persistence of the breech presentation.

(6) It is suggested that cornual implantation of the placenta may be an important factor in determining breech presentation. It is not, however, the sole cause and a breech presentation may persist irrespective of the position of the placenta; other factors such as the attitude of the foetus and the shape of the uterus presumably operate in such cases.

## Postcript

At the time when this article was in final draft, Dr. A. S. Whitehead died suddenly at the early age of 36 years. It was completed and submitted for publication by his obstetrical colleagues, who take this opportunity of acknowledging all the help they received from Dr. Whitehead and his outstanding work in obstetric radiology.

## References

Bishop, P. A. (1945): *Surg. Clin. N. Amer.* **25**, 1394.
Buxton, B. H., Hunt, R. R., and Potter, C. (1942): *Amer. J. Roentgenol*, **43**, 610.
Dippel, A. L., and Brown, W. H. (1940): *Amer. J. Obstet. Gynec.*, **40**, 986.
Gusserow (1866): *Mschr. Geburtsh. Frauenkr.*, **27**, 90.
Holzapfel, K. (1896): *Beitr. Geburtsh. Gynäk*, **1**, 286.
Reid, F. (1951): *Proc. R. Soc. Med.*, **44**, 703.
Smith, R. M. (1943): *Amer. J. Roentgenol*, **49**, 750.
Snow, W., and Powell, C. B. (1934): *Amer. J. Roentgenol.*, **31**, 37.
Snow, W., and Rosensohn, M. (1939): *Amer. J. Roentgenol.*, **42**, 709.
Stevenson, C. S. (1949): : *Amer. J. Obstet. Gynec.*, **58**, 432.
Stevenson, C. S. (1950): *Amer. J. Obstet. Gynec.*, **60**, 41.
Stevenson, C. S. (1951): *Amer. J. Obstet. Gynec.*, **62**, 488.
Torpin, R., and Holmes, L. P. (1943): *Amer. J. Obstet. Gynec.*, **46**, 268.
Vaughan, C. E., Weaver, R. T., and Adamson, D. L. (1942): *Canad. med. Ass. J.*, **46**, 314.
Whitehead, A. S. (1953): *J. Fac. Radiol.*, **4**, 245.

# EVOLUTION OF ENDOMETRIAL CARCINOMA STUDIED BY SEQUENTIAL CURETTINGS

## A Case Report

BY

M. DAVID ORRAHOOD, M.D., AND JOHN P. WYATT, M.D.

*Department of Pathology, St. Louis University, Missouri, U.S.A.*

ENDOMETRIAL cancer is pre-eminently a malignant disease beginning at the menopause or late in the fourth decade of life (Pack and Le Fevre, 1930). Previous reports of endometrial cancer in girls under 19 years of age have been documented by Hirst (1929), Hertig and Sommers (1949), and Ladinski (1915) Case 15. The example previously presented by Taussig (1925) probably represents an instance of exaggerated hyperplasia. The single report (Adams, 1916) of endometrial carcinoma in a 2½-year-old girl probably illustrates an example of mixed mesodermal tumour with dominance of epithelial development. Because of this rarity, the documentation of the following case is of value. Furthermore, tracing the development of fundic carcinoma through sequential curettings is of even greater significance, as the biopsy material offers morphological evidence of the biological steps leading to the ultimate development of endometrial cancer.

### CASE REPORT

Miss B. P., age 18, para-0, gravida-0, was admitted to the hospital at the age of 15, because of protracted bleeding at menstrual periods and copious intermenstrual bleeding. Past history revealed that this patient had suffered from measles and mumps in childhood. At the age of 12 she had been observed for "pubertal bleeding". Basal metabolic rate at that time was plus 38; a year later the basal metabolic rate was plus 14. Because of pubertal bleeding this patient received stilboestrol. The dosage was 0.5 mg. every day for 3 weeks out of 4 for a total of 6 weeks (210 mg. stilboestrol).

Physical examination on this first admission at the age of 15 was negative and curettage was performed on 27th January, 1947. Approximately 5 ml. of greyish translucent tissue was obtained. Pathological examination revealed the conventional pattern of cystic endometrial hyperplasia (Cullen's "Swiss cheese hyperplasia", Cullen, 1900) (Fig. 1). Following curettage 400 mg./hr. of radium therapy was instituted.

Despite curettement and insertion of radium the excessive bleeding continued, particularly at every third or fourth month. A severe intermenstrual haemorrhage occurred in July 1947. This girl, now aged 16, was admitted for the second time to hospital in January 1948, because of profuse vaginal bleeding of 10 days duration. Laboratory investigation revealed: a red cell count of 2,300,000 per ml.; haemoglobin 8.0 g.; white cell count of 10,700 per ml.; with a differential of stabs 5 per cent, segmented 65 per cent, lymphocytes 30 per cent. No abnormal white cells were observed in the blood smears. As a diagnosis of "bleeding disease" was entertained, further haematological investigation showed a bleeding time of 3 minutes 40 seconds, clotting time of 2 minutes, good clot retraction and numerous platelets in repeated blood smears. The serological test for syphilis (Kahn) was negative. Blood-pressure reading was 124/74. The urine was essentially negative. A second curettage was performed on 30th January, 1948, and 10 ml. of uterine scrapings were obtained. Pathological diagnosis was "adenomatous hyperplasia" (Fig. 2). This patient received 3 transfusions of 500 ml. of compatible whole blood and received heavy doses of ferrous sulphate. Testosterone was given in 50 mg. doses and discontinued after 3 days and patient discharged.

The third admission to hospital was in August 1949 because of continuing complaints of menorrhagia and metrorrhagia. Apart from small erosion on the anterior and posterior lips, physical examination was negative. The patient was subjected to a third dilatation of cervix and curettement; copious curettings were received and submitted for pathological diagnosis. The pathological histology on this material was considerably different from the material received on the two previous uterine scrapings. It was readily recognized that the histological pattern possessed many features of an atypical nature. The endometrial glands were distorted and irregular in outline and budded into the surrounding stroma. Basophilism of the cytoplasm was the common tinctorial reaction, although a number of the glands were lined with a pale swollen eosinophilic cells. The diagnosis of carcinoma *in situ* (Fig. 3)

was suggested on pathological consultation and the final diagnosis released was adenomatous hyperplasia with pronounced features of atypicality. Because of the youth of the patient, radical surgery and intensive radiation were not carried out—in the hope that the pre-cancerous alteration was reversible. Prior to discharge from hospital, patient received 1,000 ml. of compatible whole blood. The final haemoglobin reading was 12.0 g. Vaginal bleeding remained profuse and subsequently, 3 months before fourth hospital admission in July 1950, the vaginal discharge was foul-smelling. Rectal temperature readings taken over many months supported the clinical diagnosis of anovulatory menstruation. The fourth curettage was carried out on 1st August, 1950, a month before the girl's 18th birthday. Eight ml. of friable dark red tissue were received. The pathological diagnosis was invasive adenoacanthoma of the endometrium (Fig. 4). The patient submitted to radical surgery and a panhysterectomy with bilateral salpingo-oöphorectomy was performed with subsequent deep radiotherapy.

Detailed examination of the gross surgical specimen showed that approximately one-half of the thickness of the myometrium was invaded by endometrial carcinoma. The greater portion of the Fallopian tube walls shared in the polypoid carcinomatous transformation. The other interesting features were the ovarian alterations. The ovaries were studied by routine haematoxylin and eosin stain and by Heidenhain's azocarmine and Masson's trichrome. The left ovary was slightly larger than normal, measured $4 \times 2 \times 2$ cm. and had a rough, tough, white irregular fibrous capsule measuring 2 mm. and on transection presented a dense connective tissue stroma honeycombed with a moderate number of cystic structures. The majority of these structures were filled with clear fluid but one was filled with a haemorrhagic content and measured 1.5 cm. in diameter. The right ovary measured $2.75 \times 2 \times 2$ cm. and resembled the appearance of the left. The capsule was thickened and measured 3 mm. Microscopic examination showed a few follicular cysts filled with eosinophilic debris. The majority of these cysts were denuded of epithelial lining. There was a striking paucity of primordial follicles and the ovarian cortical shell was thickened due to collagenic sclerosis. No morphologic evidence of hyperoestrinism in the form of granulosa cell tumour, thecomatosis or cortical granulomatosis was encountered (Hertig, 1944). No carcinomatous implants were found in the peritoneal cavity. Several pelvic lymph nodes removed at time of operation were examined and found free of tumour. Radiographic examination of the chest revealed clear lung fields. Although no ketosteroid studies of the blood and urine were performed, the clinician and consultants in this case stated repeatedly that the girl was "pretty and feminine". No endocrinopathic evidence in the form of obesity, hirsutism or other clinical signs was uncovered. At the moment of writing, the patient, married shortly after her 18th birthday, is in good health, with no detectable evidence of cancer.

## Discussion

The changing pre-cancer profile of cystic hyperplasia, adenomatous hyperplasia and carcinoma *in situ* has been stressed previously by Hertig and Sommers (1949). In this instance, the gradual development of uterine carcinoma was revealed through repeated biopsies, but the nature of the initiating process or the factors responsible for the relentless progress to the end phase of adenoacanthoma remain hidden. Hertig and Sommers (1949), in their admirable discussion on this very problem, indicated that radiation therapy probably possessed a greater carcinogenic influence than administered oestrogens. From the experimental approach, the studies of Greene and Saxton (1938) on the uterine adenomata of rabbits support the transitional development of uterine carcinoma in that a genetic influence apparently swings experimental uterine tumours into endometrial carcinoma within a period of several years. In this example, the radiation dosage was quite low, and represents the minimal dosage given to cases of metropathia haemorrhagica. Again, the total amount of stilboestrol was not excessive, 0.5 mg. every day for 3 weeks out of 4 for a total of 6 weeks (210 mg. stilboestrol) (Speert, 1948). Furthermore, from the point of time, 3 years elapsed after the receipt of hormonal-radiation therapy before endometrial cancer was observed. Nevertheless in this instance the time interval between the appearance of Cullen's hyperplasia and frank endometrial cancer was much less than has been previously reported (Hertig and Sommers, 1949). On the other hand, the adenoacanthoma of the fundus showed no secretory activity as might conceivably be expected if excessive exogenic stilboestrol was playing a continuing role. Because of the little factual support available, the role of the exogenic factors of radiation or hormonal therapy in initiating or even accelerating the irreversible endometrial cancer, remains conjectural and debatable.

The pathological alterations in the ovary were of interest. The thickened capsule, the presence of multiple, small follicular cysts, and the paucity of primordial follicles and atretic corpora lutea are the findings usually associated with the sclerocystic ovaries of older women.

The presence of large, pale ovaries may in

FIG. 1

Cystic endometrial hyperplasia generally distributed through curettings. Patient aged 15 years. Hematoxylin and eosin. ×135.

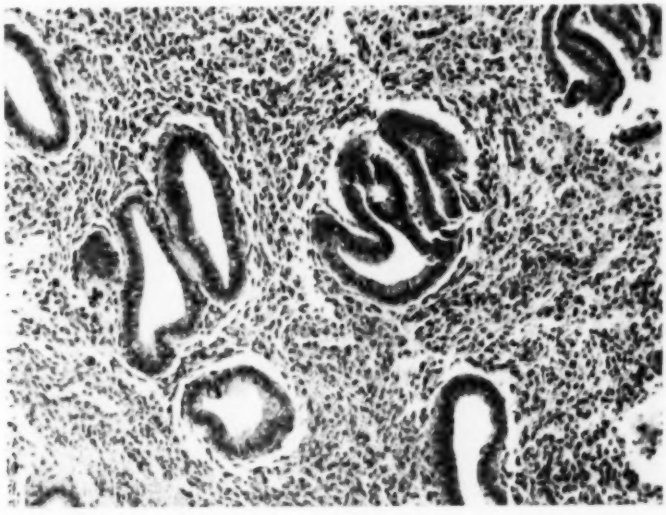


FIG. 2

Same patient, aged 16 years. Curettings showing adenomatous hyperplasia of well differentiated endometrial glands. Hematoxylin and eosin. ×125.

M.D.O. & J.P.W.

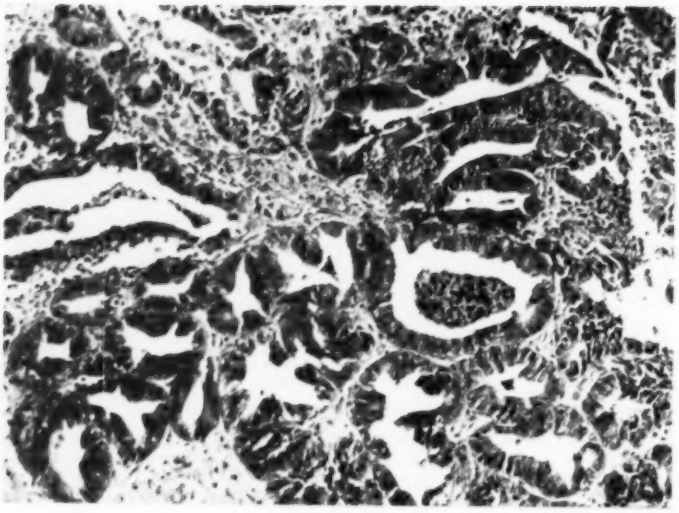


FIG. 3

Same patient, aged 17 years. Diffuse adenomatous hyperplasia with features of atypicality and anaplasia. Hematoxylin and eosin. ×135.

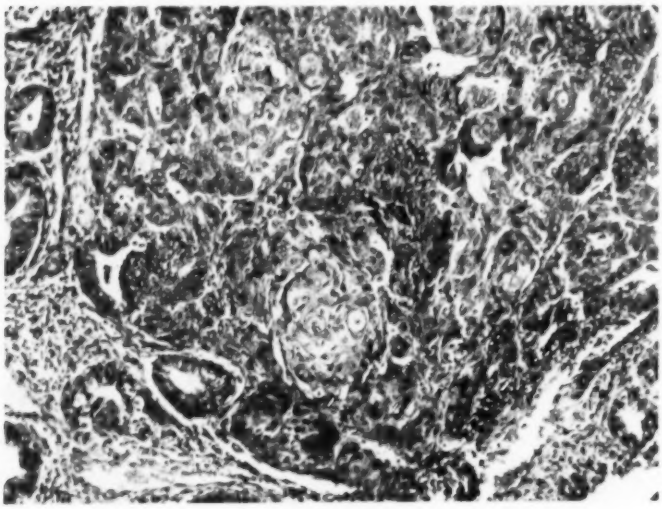


FIG. 4

Same patient, aged 17 years, 4 months after previous curettage. Adenocarcinoma of endometrium with stromal invasion and atypical squamous metaplasia. Hematoxylin and eosin. ×130.

some instances be associated with endocrine imbalance. This cystic alteration of the ovary, originally described by Schröder (1915), may be co-existent with endometrial hyperplasia, described as " Swiss cheese " hyperplasia. In a few instances of sclerocytic disease of the ovaries, a symptom complex, sometimes referred to as the Stein-Levinthal syndrome (Stein and Levinthal, 1935), associated with evidence of masculinization, has been separated. Although the ovaries of this 18-year-old girl showed cortical fibrosis and follicular cysts, there was no clinical evidence of hormonal upset, such as alterations in secondary sex characteristics. The role of the pituitary-adrenal axis cannot be evaluated, as biochemical investigations were not carried out.

## Summary

Through sequential biopsies, the morphological transition of cystic endometrial hyperplasia through adenomatous hyperplasia into carcinoma *in situ* and eventually adenoacanthoma of the uterine body has been studied. The exogenic and possible endogenic factors concerned in this case are briefly discussed. The unusual ovarian alterations associated with " evolutionary " cancer are stressed.

We are indebted to Dr. E. T. Huber for his kind permission to utilize this case material.

## References

Adams, J. E. (1916): *Proc. R. Soc. Med.*, **9**, Sect. Obstet. Gynaec., 45.

Cullen, T. S. (1900): *Cancer of the uterus. Its pathology, symptomatology, diagnosis and treatment, also the pathology of diseases of the endometrium.* London.

Greene, H. S. N., and Saxton, J. A., jr. (1938): *J. exp. Med.*, **67**, 691.

Hertig, A. T. (1944): *Endocrinology*, **4**, 581.

Hertig, A. T., and Sommers, S. C. (1949): *Cancer*, **2**, 946.

Hirst, B. C. (1929): *Amer. J. Obstet. Gynec.*, **18**, 104.

Ladinski, L. J. (1915): *Surg. Gynec. Obstet.*, **20**, 325.

Pack, G. T., and Le Fevre, R. B. (1930): *J. Cancer Res.*, **14**, 167.

Schröder, R. (1915): *Arch. Gynäk.*, **104**, 27.

Speert, H. (1948): *Cancer*, **1**, 584.

Stein, I. F., and Levinthal, M. L. (1935): *Amer. J. Obstet. Gynec.*, **29**, 181.

Taussig, R. J. (1925): *Surg. Clin. N. Amer.*, **5**, 1437.

# TRANSPLANTATION OF THE OVARY INTO THE UTERINE CAVITY FOR THE TREATMENT OF STERILITY IN WOMEN

BY

P. G. PRESTON, M.B., Ch.B., F.R.C.O.G.

*Nairobi, Kenya*

MY first interest in the transplantation of the ovary into the uterine cavity was first aroused in 1927 when I was a house surgeon to the late Mr. J. Eric Stacey at the Jessop Hospital for Women in Sheffield. It happened that one night we operated upon a young woman for a ruptured ectopic gestation which necessitated the removal of her one remaining Fallopian tube, as the unfortunate patient had undergone a similar tragic experience a year before. As the patient was very anxious to have children Mr. Stacey incised the uterus and pushed one ovary into the cavity and sutured it into position afterwards closing the wound in the uterus. He remarked at the time that he only knew of one such operation which had been successful and that had been performed by a French surgeon and added that this was the only chance that this patient had of bearing her own child.

I have investigated the literature on this subject—going back as far as the year 1920, and I can find comparatively little written as regards the transplantation of the ovary into the uterine cavity with the intention and result of producing pregnancy. Most of the literature is written in foreign languages. I have, therefore, had to depend upon other people's quotations of this literature.

The only British contribution is that of Solomons (1931), but his article only describes the transplantation of the ovary from one woman into the uterus of another, and this was done to relieve severe premature menopausal symptoms caused as a result of a bilateral oöphorectomy and no actual pregnancy is recorded.

Sippell (1924), Schreiner (1927), Simeéch (1930), Risley (1935), Panis (1937), Slovak (1939), and Moraes (1949), all report cases of pregnancy following the transplantation or transposition of the ovary into the uterine cavity, whilst Van der Elst (1933) was apparently so thrilled with a result of his that it was published both in Belgium and America!

Other authors who have contributed to the literature on the subject are Magian (1931), Riona (1931), Cotta (1936), and Geyer (1941); whilst Le Lorier, Lapeyre and Mayer (1932) and Garrow (1937) review the literature.

Perhaps the best article is that of Estes and Heitmeyer (1934) who review the literature and give a description of their operation and results. They state that one of the earliest attempts to obtain pregnancy after salpingectomy was that of Robert Morris in 1895, who, after a radical removal of both the Fallopian tubes and ovaries, transferred or grafted a piece of ovary into the interior stump of one oviduct. One month later the patient became pregnant and aborted at the end of the third month.

Franek in 1898 records 3 cases; 1 woman aborted, 1 had an extra-uterine pregnancy, and 1 had a full-time child.

In 1900 M. Palmer Dudley described an operation which is similar to the one that I have been in the habit of performing. The procedure is to open up the fundus of the uterus, and the ovary, still attached to its pedicle, is placed in the uterine cavity (which Dudley describes as "dangling like a polypus"), and the uterus is closed above the pedicle. The patient aborted after 2 or 3 months.

In 1908 Petit successfully transplanted a quarter of the left ovary in a woman of 32 years of age and she was delivered of a full-time child 2 years later.

In 1915 Storer and in 1922 Cullen Unterberger describe similar cases which became pregnant, but unfortunately these terminated in abortions around 3 months.

Bainbridge in America in 1923 records a case who, 1½ years after transplantation of a small portion of an ovary, bore a healthy child.

Aleson between 1827 and 1934 operated upon 8 cases. In 1 case an abortion occurred, and another patient became pregnant, but at about 8 months of gestation her uterus ruptured at the site of the transplantation.

Foster in 1930 records that he grafted a " free ovary ", and of 18 patients 3 had full-time pregnancies.

In 1934 Estes and Heitmeyer record that they had been performing the operation of implantation of the ovary in which " the cut surface of the remaining ovary still attached to its pedicle is implanted upon the cut surface of the uterine horn ", following a bilateral salpingectomy and a unilateral oöphorectomy. Of 50 patients whose case records are complete, 4 became pregnant (8 per cent), 2 had abortions at about the third month, 2 had full-time pregnancies. Of these latter, 1 woman had but a single child, and the other had 3 full-time live children and 1 stillborn child.

Franklin H. Martin in 1903 describes 1 case, Pratt in 1926 describes 4 cases, and Sheroff in 1926 describes 2 cases, none of which became pregnant.

I only perform this operation in patients who have previously lost both Fallopian tubes, or whose tubes are so badly damaged that it is impossible either to perform a salpingostomy or to excise the damaged uterine end and transplant the otherwise healthy portion of the tube into the uterine cavity through the cornu. Another condition influencing the decision to perform this operation is that at least one ovary must be fairly healthy and preferably not cystic, or the less cystic the better it is.

The patient is duly informed that no success can be guaranteed as a result of the operation, but that the possibility of pregnancy occurring is not very remote.

After opening the abdomen the ovaries are examined and the healthier one is usually used. I always make certain that the ovary is sufficiently mobile to allow it to be inserted into the uterine cavity without undue tension on its pedicle, and if necessary it is immobilized sufficiently to overcome any undue tension. A loose No. 1 catgut ligature is then placed around the ovarian end of the pedicle and the ends are left long. An incision is then made through the posterior wall of the fundus of the uterus, long enough to admit the ovary which is then pushed through the incision into the uterine cavity. The ends of the catgut are then severally threaded on to a fine needle and taken through the uterine cavity and posterior wall, one on either side of the incision, and tied off, thereby anchoring the ovary in position inside the uterine cavity and at the same time partially closing the incision. The uterine incision is then loosely closed by means of interrupted catgut sutures and the abdomen closed in the usual manner.

As a rule patients show very little reaction to this operation.

Since 1944 I have performed this operation upon 21 women (1 European, 3 Asians, and 17 Africans):

| | European | Asian | African | Total |
|---|---|---|---|---|
| 1944 | – | 1 | – | 1 |
| 1946 | – | 2 | 6 | 8 |
| 1947 | – | – | 8 | 8 |
| 1948 | – | – | 2 | 2 |
| 1951 | 1 | – | 1 | 2 |
| | 1 | 3 | 17 | 21 |

Two of these were performed the year before last so perhaps it is a little early to anticipate results from these. Of all the cases I have been unable to trace 11. Of the 10 cases which I have been able to follow up, 3 have become pregnant. One, an Asian lady, terminated in a very early abortion. One African, who was operated upon in September 1946, gave birth normally to a full-time male child in November 1947, a full-time female child in August 1949, aborted a 3-months pregnancy in March 1951, and gave birth to another child about February 1952. The third patient, an African who was operated upon in January 1947, was delivered at Punwani Maternity Hospital by means of a Caesarean section in June 1951 by my friend Dr. Candler. The Caesarean section was performed because of the abnormal lie of the foetus, which at the time was thought to be due to the fact that the patient had undergone a ventro-suspension of

the uterus which was causing an abnormal lie of the uterus.

The percentage of successful results in the total number of patients operated upon is 14.28, whereas the percentage of success in only those which I have been able to follow up is as high as 30.

The percentage of patients who actually went to full time and produced live babies of the total number operated upon is 9.52 and of those actually traced is 20.

### References


Cotta, G. (1936): *Rev. franç. Gynéc. Obstét.*, **31**, 913.

Van der Elst (1933): *Le Scalpel*, **86**, 1150; *J. Chir. Belge*, **32**, 62.

Estes, W. L., jr., and Heitmeyer, P. L. (1934): *Amer. J. Surg.*, **24**, 563.

Garrow, F. (1937): *Rass. Obstet. Ginec.*, **46**, 460.

Geyer, M. (1941): *Atti Soc. ital. Obstet. Ginec.*, **37**, 53.

Le Lorier, Lapeyre, J. L., and Meyer, M. (1932): *Bull. Soc. Obstét. Gynéc.*, **21**, 166.

Magian, A. C. (1931): *Bull. Soc. Obstét. Gynéc.*, **20**, 119.

Moraes, A. de (1949): *Ann. brasil. Ginec.*, **28**, 347.

Panis, G. (1937): *Mem. Acad. Chir., Paris*, **63**, 686.

Riona, A. (1931): *Zbl. Gynäk.*, **56**, 3516.

Risley, E. H. (1935): *Maine med. J.*, **26**, 189.

Schreiner, R. (1927): *Dtsch. med. Wschr.*, **53**, 2084.

Simeéch, J. (1930): *Cas. Lék. ces.*, **96**, 1157.

Sippell, P. (1924): *Zbl. Gynäk.*, **48**, 15.

Slovak, F. W. (1939): *Amer. J. Obstet. Gynec.*, **38**, 342.

Solomons, B. (1931): *J. Obstet. Gynaec. Brit. Emp.* **38**, 324.

# A CASE OF THE STEIN-LEVENTHAL SYNDROME ASSOCIATED WITH CARCINOMA OF THE ENDOMETRIUM

BY

R. D. DE VERE, F.R.C.S., M.R.C.O.G.

*Registrar, Department of Obstetrics and Gynaecology*

AND

K. R. DEMPSTER, M.B., B.S.

*Assistant Pathologist*

*St. Thomas's Hospital Medical School, London*

THE object in describing this case is to draw attention to a condition which has received little mention in British medical literature, and to illustrate its possible association with endometrial carcinoma. Although there have been several series of cases of the Stein-Leventhal syndrome published in America since the condition was first described in 1935, its association with endometrial carcinoma receives only passing mention, except in one paper (Dockerty, Lovelady and Foust, 1951) which deals primarily with carcinoma of the endometrium rather than with the Stein-Leventhal syndrome itself.

To quote Stein (1945), the syndrome is characterized clinically by "menstrual irregularity, amenorrhoea, a history of sterility, a masculine type of hirsutism and, less consistently, by retarded breast development and obesity." This symptom complex is associated with the presence of bilateral enlarged polycystic ovaries in which ovulation is absent or only occasional.

## CASE HISTORY

J. L., aged 23, was married 6 months and nulliparous. She complained of irregular periods for 8 years, for the last 5 months of which they had become prolonged, excessive and painful. There was nothing of significance in her past medical history.

*Menstrual history.* Her periods started at the age of 13 and were regular, lasting 3 to 4 days, every 28 days, until the age of 15. From 15 to 20 she had almost complete amenorrhoea with a very scanty loss every 6 months or so. From 20 to 23 the loss became gradually more prolonged, lasting from 2 days to 6 weeks, every 2 to 3 months, but the loss was never excessive. In the 5 months before her attendance at hospital she had 3 episodes of bleeding lasting 1, 6 and 4 weeks respectively. These losses were heavy and associated with the passage of clots.

Libido was normal and she complained of only slight occasional dyspareunia. She stated that there had been a gradual increase in the growth of hair on her face, chest, abdomen and legs since puberty, but she was unable to say whether this had increased more rapidly in recent years.

*Examination.* She was well covered but not markedly obese. There was a moderately thick growth of hair on her face, chest, abdomen, buttocks and legs. The distribution of pubic hair was of the male type. Her breasts were normally developed and there was no hyperplasia of the external genitalia. Pelvic examination revealed a normal-sized, anteverted uterus with no other pelvic masses. The blood-pressure was 120/80. No abnormality was found on examination of the heart, lungs and central nervous system.

*April* 1952. Examination under an anaesthetic confirmed that the uterus was normal in size and anteverted, and a left ovarian tumour the size of a duck's egg was also palpable and was thought to be a follicular cyst. It was freely mobile. No tumour was found in the right fornix. Curettage produced a large quantity of oedematous endometrium.

*Histology.* Some pieces of tissue showed the typical appearances of cystic hyperplasia of the endometrium. Elsewhere there was great proliferation of the glandular epithelium with only a very thin core of stroma intervening between the glands. The epithelial cells varied in shape and size and numerous mitoses were present. Squamous metaplasia was apparent. The appearances were thought to suggest an early carcinomatous change (Fig. 1).

*Laparotomy* (performed one week later). The abdomen was opened through a mid-line subumbilical incision. Both ovaries were found to be enlarged, the left measuring 8×3.5 cm. and the right 6×2.5 cm. They were kidney-shaped, greyish in colour, and multicystic. The capsule was obviously thickened. There were no adhesions to surrounding structures and the other pelvic organs were normal in all respects. A longitudinal wedge resection of each ovary was performed during which approximately half of each ovary was removed. The ovaries were reconstituted with continuous atraumatic catgut sutures.

*Histology*. Investing the ovaries was a layer of hyalinized fibrous tissue approximately 1 mm. in depth. In the ovarian cortex beneath this layer, there was a noticeable scarcity of primordial follicles, and most of those present appeared to be degenerating. Of the 30–40 counted in 3 sections, only 1 was maturing normally. Seventeen cysts were found in the 3 sections prepared; 4 were lined by granulosa cells with luteinization of the theca interna (Fig. 2), 7 were theca luteal cysts, and the remaining 6 were follicle cysts of long standing with disappearance of the granulosa cells. Corpora lutea were absent. Only a small amount of ovarian hilum was present, and no "hilus cells" were seen.

The patient made an uneventful recovery from operation. Following her discharge from hospital she had a scanty period lasting 2 days followed by 3 similarly scanty periods at intervals of 2 months, 2 weeks, and 1 month. She felt better in herself than before operation.

*October* 1952. Further curettage was performed and again a large quantity of bulky tissue was obtained. Both ovaries were palpable and enlarged to about 3 times their normal size. Most of the tissue on histological examination showed undoubted columnar celled adenocarcinoma of the endometrium (Fig. 3). There were still a few small pieces of non-malignant tissue and these showed a normal non-secretory endometrium without cystic hyperplasia.

One week later, total hysterectomy with bilateral salpingo-oöphorectomy was performed.

*Pathology*. The uterus measured 7.5 cm. from the fundus to the external os and appeared normal externally. When opened to show the cavity the cervix was seen to contain several small cysts adjacent to the upper part of the cervical canal. The cavity of the body of the uterus contained a mass of white friable material with an irregular surface arising from the whole area of the endometrium. There was no macroscopical evidence of invasion of the muscular wall. The Fallopian tubes appeared normal. The ovaries were enlarged to approximately the same degree, the right ovary measuring $6 \times 3.5 \times 2.5$ cm. The surface was white and for the most part smooth, and many cysts were present. The cut surface of both ovaries showed a background of pale tissue with dark brown mottling and numerous spherical cysts, the largest measuring 1 cm. in diameter. Most of these cysts contained pale yellow watery fluid, but a few contained brown fluid due to admixture with blood. A corpus luteum appeared to be present in the right ovary (Fig. 4).

*Histology*. The cervix appeared normal except for several distended glands. The body of the uterus showed a columnar celled adenocarcinoma of the endometrium with prominent squamous metaplasia (Fig. 5). There was only slight invasion of the myometrium which was otherwise normal. The appearance of the ovaries was similar to that described in the ovarian tissue removed by wedge resection. Of the 35 cysts present in one longitudinal section from each ovary, 23 were theca luteal cysts, 4 were lined by granulosa cells only, and 8 were old follicle cysts, the granulosa cells having disappeared. The corpus luteum in the right ovary had degenerated and consisted of a convoluted band of hyaline material, in which no cells survived, surrounding an area of loose connective tissue. A considerable amount of ovarian hilum tissue was present and "hilus cells" were found in association with autonomic nerve fibres in each ovary.

The patient was last seen in January 1953 when she felt well except for moderate menopausal symptoms for which small doses of Stilboestrol were prescribed. Pelvic examination revealed no abnormality.

## Discussion

The symptoms, signs and pathological findings in this case are typical of the Stein-Leventhal syndrome, that is, a normal menarche followed by amenorrhoea and hirsutism in a young woman with bilateral polycystic ovaries. As Greenblatt (1951) stresses, hirsutism is the only masculinizing feature and the patients themselves are completely feminine in every other respect. Absence of enlargement of the clitoris, voice changes, hypertension, glycosuria and abnormal urinary 17-ketosteroids helps to distinguish these cases from the adreno-genital syndrome, Cushing's disease, and masculinizing tumours.

The demonstration of enlarged ovaries may not be possible on clinical examination and, of 21 cases reported by Ingersoll and McDermott (1950), it was possible in only 6. Stein strongly advocates the use of pelvic "pneumoroentgenography", and culdoscopy is recommended by Ingersoll and McDermott. While these measures may appear drastic the excellent results obtained by wedge resection of the ovaries makes it important to detect ovarian enlargement in such cases.

Typically, and as in the case described, the ovaries are enlarged to 3 or 4 times their normal size but rarely more. They are kidney-shaped and greyish in colour with numerous small cysts containing clear fluid filling the cortex. On incising the tunica it is found grossly thickened. Microscopically, the cysts are follicular in type, usually with persistence of granulosa cells in 1 or more layers. Hyperplasia and luteinization

FIG. 1

Endometrium obtained at first curettage (April 1952), showing cystic hyperplasia, and atypical adenomatous hyperplasia highly suggestive of carcinoma. H. and E. ×42

R.D.deV. & K.R.D.

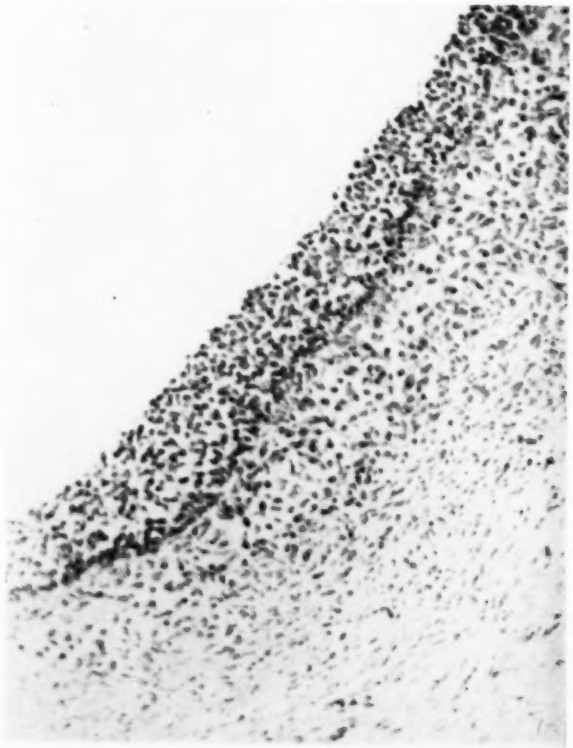


FIG. 2

Portion of wall of theca-lutein cyst of ovary, showing well-marked luteinization and hyperplasia of theca interna cells. H. and E. ×140

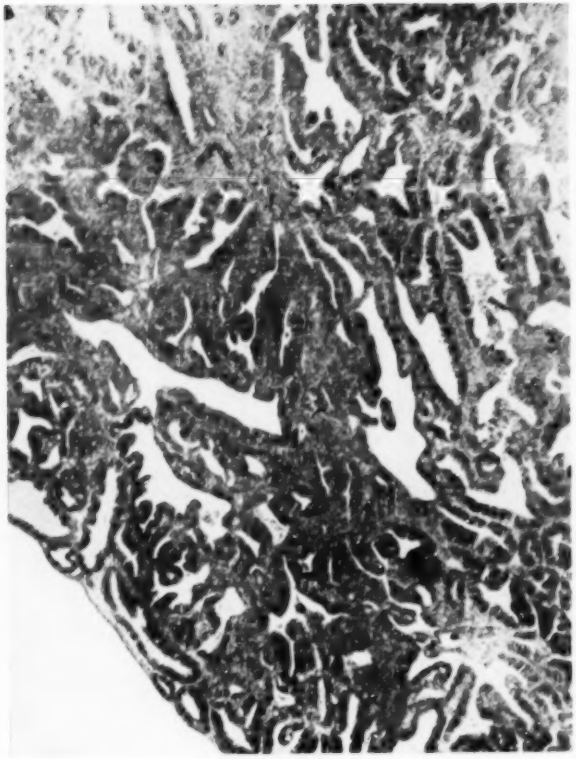


FIG. 3
Endometrium obtained at second curettage (October 1952).
H. and E. ×42

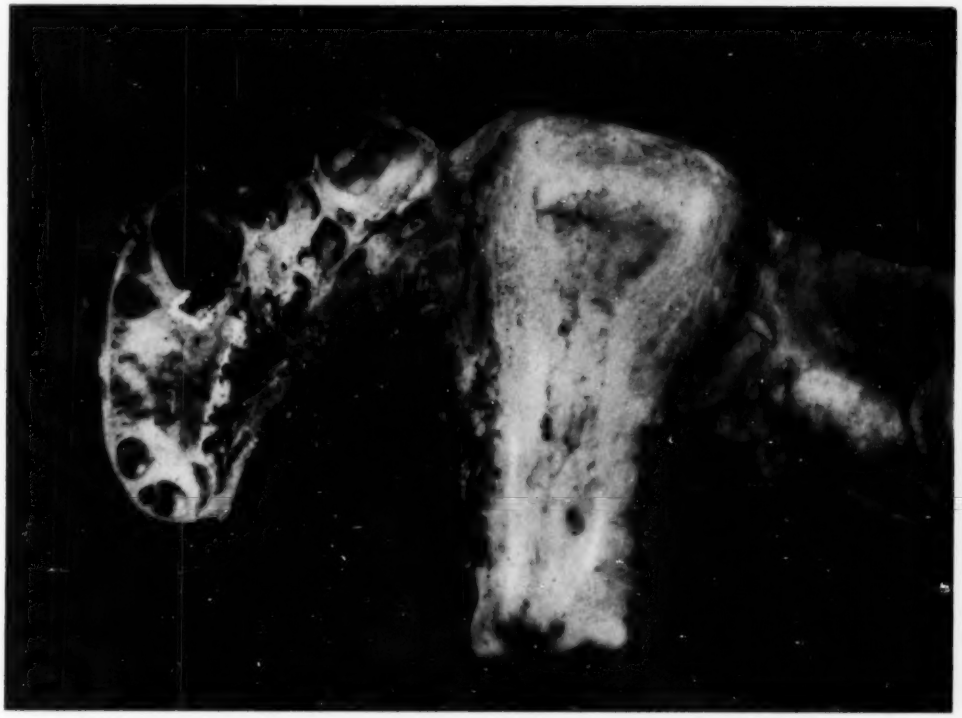


FIG. 4

Uterus, with uterine cavity exposed, and right ovary.
Note the position of the corpus luteum.

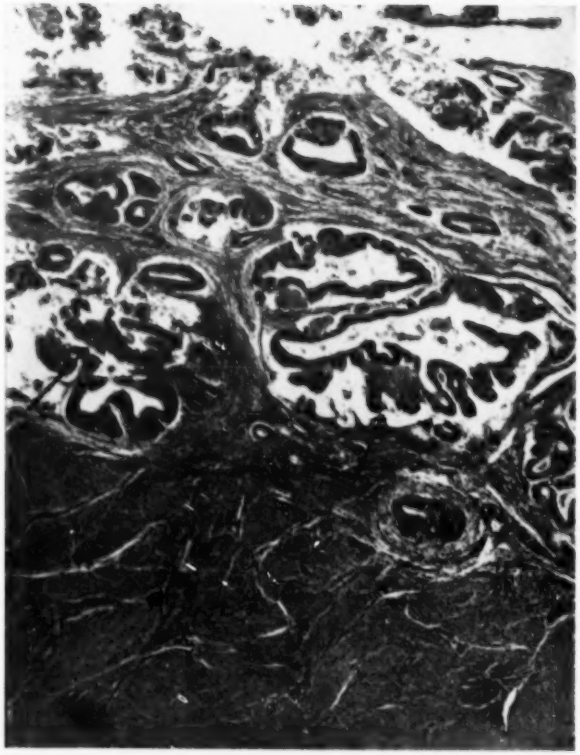


FIG. 5
Endometrium and portion of myometrium from hysterectomy specimen. Note squamous metaplasia. H. and E. ×42

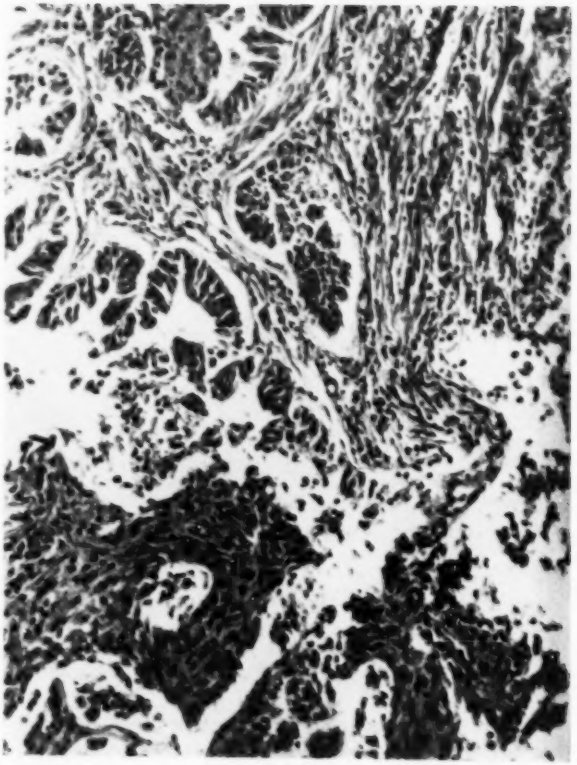


FIG. 6
Endometrium from hysterectomy specimen, showing squamous metaplasia. H. and E. ×140

of the theca interna cells is striking (Leventhal and Cohen, 1951). Corpora lutea are rarely found, and Stein suggests that if present they may follow rupture of a follicle into an adjacent cyst. The position of the visible corpus luteum, as shown in Fig. 4, suggests that this has occurred.

The aetiology of the condition is unknown, but Stein believes it to be due to hormonal imbalance between the anterior pituitary and the ovary, and that the symptoms of amenorrhoea and sterility may be due to fibrosis of the ovarian capsule preventing ovulation. This theory is supported by the resumption of ovulation and regular menstruation which usually follows wedge resection of the ovaries. Ingersoll and McDermott (1950) could demonstrate no increase in circulating follicle stimulating hormone in their cases. As these patients usually have a period of normal menstruation following the menarche it is unlikely to be congenital and the microscopical appearance of the ovaries is against an inflammatory aetiology. It is suggested by Culiner and Shippel (1949) that the hirsutism is the result of the androgenic effect of luteinization of the theca interna.

As would be expected from the absence of ovulation, the endometrium is typically non-secretory (Ingersoll and McDermott, 1950), but it may show cystic hyperplasia or even atypical adenomatous hyperplasia (Sommers, Hertig and Bengloff, 1949). Dockerty, Lovelady and Foust (1951), in investigating 36 cases of endometrial carcinoma in young women, found that 7 of these cases showed at least 4 of the main features of the Stein-Leventhal syndrome. In view of the squamous metaplasia present in the case under discussion (Figs. 5 and 6), it is also interesting that 10 of their cases were adeno-acanthomata. They stress the possibility of the presence of endometrial carcinoma in hirsute young women with menstrual irregularity.

The conservative treatment of this case in the first instance was based on the hope that the atypical histological appearance of the endometrium might still be reversible. However, the failure of ovarian wedge resection to restore a normal menstrual rhythm, and the obviously malignant character of the curettings obtained 5 months later made further conservative treatment unjustifiable.

## Conclusion

While no conclusion can be drawn from a single case, it is of interest that endometrial carcinoma at such an early age should be associated with the Stein-Leventhal syndrome. According to Dockerty, Lovelady and Foust (1951), this association appears to be not uncommon. Whether carcinoma occurs as a result of cystic hyperplasia is a question on its own (Novak and Yui, 1936), and unfortunately Dockerty *et al.* (1951) do not say whether cystic hyperplasia was present in their cases prior to the development of the carcinoma.

We believe that the gradual transition of the endometrial histology in this case from cystic hyperplasia through atypical adenomatous hyperplasia to frank carcinoma is secondary to the presence of the Stein-Leventhal syndrome, and that this association in young women may be more common than is generally realized.

We would like to thank Mr. A. J. Wrigley for permission to publish this case, and Dr. J. Bamforth for his help in the preparation and interpretation of the pathological material. Our thanks are also due to Mr. A. E. Clark for the photographs.

A contribution towards the expenses of this research was made from the Endowments Fund of St. Thomas's Hospital.

## References

Culiner, A., and Shippel, S. (1949): *J. Obstet. Gynaec. Brit. Emp.*, **56**, 439.

Dockerty, M. B., Lovelady, S. B., and Foust, G. T. (1951): *Amer. J. Obstet. Gynec.*, **61**, 966.

Greenblatt, R. B. (1951): *Postgrad. Med.*, **9**, 492.

Ingersoll, F. M., and McDermott, W. V. (1950): *Amer. J. Obstet. Gynec.*, **60**, 117.

Leventhal, M. L., and Cohen, M. R. (1951): *Amer. J. Obstet. Gynec.*, **61**, 1034.

Novak, E., and Yui, E. (1936): *Amer. J. Obstet. Gynec.*, **32**, 674.

Sommers, S. C., Hertig, A. T., and Bengloff, H. (1949): *Cancer*, **2**, 957.

Stein, I. F. (1945): *Amer. J. Obstet. Gynec.*, **50**, 385.

Stein, I. F., and Leventhal, M. L. (1935): *Amer. J. Obstet. Gynec.*, **29**, 181.

# PREGNANCY AND POLYCYSTIC DISEASE OF THE KIDNEYS

BY

W. GORDON MILLAR, M.B., M.R.C.O.G.

*Senior Registrar, Obstetrics and Gynaecology*
*Royal Maternity Hospital and Royal Samaritan Hospital, Glasgow*

THERE is a paucity of reports on the occurrence of polycystic disease and pregnancy, and opinions on the management of such cases are divided. Crabtree (1942) collected 11 cases from the literature and added 1 further case that had been the only one found among the studied urological cases at the Boston Lying-in Hospital for 20 years. Further single cases have been reported by Branham (1947), Brugsch and Brodie (1948), Findley (1947), and Callaghan (1950). Morris (1952) described 4 cases.

Five cases have been diagnosed in the Royal Maternity Hospital, Glasgow, over the last 20 years.

Polycystic disease is slightly more common in women than in men. Almost invariably the condition is bilateral and in approximately 20 per cent of cases a cystic condition of other organs is present, particularly the liver, pancreas, and lungs. In 1 of the 5 patients in the present series the liver was also grossly enlarged due to polycystic disease.

In a few cases the disease has been regarded as unilateral, but removal of the obviously affected kidney has been followed many years later by the finding that the remaining kidney has become grossly enlarged owing to polycystic disease.

There is a strong hereditary tendency exhibited by the disease and its occurrence in 4 successive generations has been recorded (Crawford, 1933). Cannon (1947) showed that 2 women in one family with polycystic kidneys transmitted the disease to 5 out of 9 children.

In the foetus the grossly enlarged kidneys may cause dystocia (Bourland, 1946), and about a third of the babies born with the condition are stillborn or die in early childhood from anaemia. Among those whose renal condition is not demonstrable in childhood, growth of the cysts and loss of renal function are usually slow and symptoms are delayed until the fourth or fifth decade, when death occures from uraemia. In younger women, the occurrence of a pregnancy with renal complications or hypertension may throw light on a disease hitherto remaining "latent".

Rall and Odel (1949), in a review of 207 cases of polycystic disease occurring in both sexes, found that hypertension was present in over 75 per cent. The degree of hypertension depends on the amount of kidney destruction. The pressure of the cysts leads to atrophic changes in the compressed renal parenchyma and the larger and more cystic the kidneys are, the more marked is the interstitial nephritis.

The clinical features of the 5 cases occurring in the Royal Maternity Hospital are summarized below:

*Case 1* was aged 26 years, in her second pregnancy. In her first pregnancy in 1931 labour was induced at 36 weeks on account of hypertension and albuminuria. The child was stillborn. Her second pregnancy occurred in 1932 and she was admitted to hospital when 33-weeks pregnant on account of severe vomiting for 24 hours. On admission she was drowsy and looked ill. The blood-pressure was 250/170. There was no albuminuria. Convulsions preceded death from uraemia 2¼ hours after admission. Autopsy revealed bilateral gross polycystic disease of the kidneys and generalized arterio-sclerosis.

*Case 2* was aged 25 years and in her second pregnancy. Her father had died from polycystic disease of the kidneys. In her first pregnancy in 1935 eclampsia had occurred at 24 weeks. Blood-pressure at that time was 175/110. Labour was induced without success and, at the 26th week of pregnancy, the blood-pressure rose to 220/150 and eclamptic seizures recurred. Abdominal hysterotomy was performed under local anaesthesia, and the presence of bilateral polycystic kidneys was discovered. Severe urinary

FIG. 1

*Case* 4. Intravenous pyelogram showing marked elongation of the whole pelvic outline and of the calyces. The excretion of the dye is good.

FIG. 2

*Case* 4. Bilateral retrograde pyelogram showing similar appearances.

W.G.M.

FIG. 3
*Case* 5. Intravenous pyelogram showing good kidney function. The arrow points to the suspicious scattering of the dye at the lower pole of the right renal pelvis.

FIG. 4
*Case* 5. Bilateral retrograde pyelogram showing an absolutely typical picture of polycystic disease.

tract infection occurred in the post-operative period. On dismissal from hospital three weeks after operation, albuminuria was still present, but the blood-pressure had fallen to 110/70. She was admitted to hospital at the tenth week of her second pregnancy in March 1936. The blood-pressure was 170/120 but there was no albuminuria. Abdominal hysterotomy and sterilization were performed and exploration at the time of operation confirmed the presence of bilateral large polycystic kidneys.

*Case 3*, aged 33 years, was in her first pregnancy. She was admitted to hospital in September 1946 when 12-weeks pregnant on account of pain in the right loin and right side of her abdomen associated with frequency of micturition. The right kidney was enlarged and tender. The blood-pressure was 140/78 and there was slight albuminuria and pyuria. The blood urea was 35 mg./100 ml.; this dropped to 18 mg./100 ml. after 2 weeks. Intravenous and retrograde pyelograms showed changes pathognomonic of bilateral polycystic disease of the kidneys. Her condition improved with treatment, the renal function appeared to be satisfactory, and the pregnancy was allowed to continue. She was re-admitted to hospital when 38-weeks pregnant. The blood-pressure was 140/90, slight pyuria persisted and labour was induced by artificial rupture of the membranes. Spontaneous delivery of a live, healthy child occurred and in the puerperium the urinary infection rapidly responded to treatment.

*Case 4*, aged 26 years, was in her first pregnancy. She attended the hospital for the first time in October, 1952, when 3-months pregnant. The blood-pressure was 195/120 and abdominal examination revealed the presence of enormous masses in both kidney regions. Intravenous and retrograde pyelograms confirmed the presence of bilateral polycystic kidneys (Figs. 1 and 2). Renal function was not apparently impaired; the blood urea was 25 mg./100 ml. The urine at this stage showed no abnormality, but urinary infection and haematuria recurred from the fourth month until delivery.

Her condition deteriorated and, when 30-weeks pregnant, her blood-pressure had risen to 240/130. The urine contained 9 g. albumin/litre, there were white patches on the left retina and a slight mixed accidental haemorrhage occurred. Labour was induced by instrumental dilatation of the cervix and puncture of the forewaters on 12th February, 1953, and she delivered a stillborn child weighing 2 pounds 3 ounces, 27 hours after induction. Postmortem examination of the child did not reveal any renal abnormality. She was dismissed on 4th March, 1953, the 19th day of the puerperium. The blood-pressure was now 160/105 and the urine contained 1 g. albumin per litre. She last reported on 22nd March, 1953, and was feeling quite well although the blood-pressure was 210/105 and the urine contained a trace of albumin.

As far as the patient was aware, there was no known instance of polycystic disease in the other members of her family.

*Case 5*, aged 42 years, was in her eighth pregnancy. Her 7 previous pregnancies had been entirely uncomplicated, all the children are alive and well, and in none was there a history of polycystic kidneys. In 1949 a laparotomy was performed because of a long history of dyspepsia and the presence of an epigastric mass. This revealed an enormous polycystic liver and bilateral polycystic kidneys. A duodenal ulcer was also present which responded afterwards to medical treatment. Liver biopsy was performed and histological examination showed the changes typical of polycystic disease. She first attended this hospital in the third month of her present pregnancy on 12th March, 1953. She had no abnormal symptoms, the blood-pressure was 110/74 and there was no pyuria or albuminuria. On abdominal examination, the lobulated edge of the polycystic liver was palpable a full hand's breadth below the costal margin, and both kidneys were palpably enlarged.

An intravenous pyelogram showed appearances suggestive of polycystic disease on the left side, but on the right side there was a suspicious scattering of the dye at the lower pole of the renal pelvis (Fig. 3). Bilateral retrograde pyelography, however, showed the changes typical of polycystic disease (Fig. 4). There was no apparent impairment of renal function, urinalysis was normal and the blood urea was 22 mg./100 ml.

| | |
|---|---|
| Total plasma proteins ... | 5.96 g/100 ml. |
| Albumin ... ... | 3.96 g/100 ml. |
| Globulin ... ... | 1.70 g/100 ml. |
| Fibrinogen ... ... | 0.30 g/100 ml. |
| Serum alkaline phosphatase | 3 units/100 ml. |
| Plasma bilirubin ... ... | 0.2 mg./100 ml. |

Her most recent visit to the hospital clinic was on 28th April, 1953. She was then 18-weeks pregnant and felt quite well. The blood-pressure was 110/70 and urinalysis was normal.

## Discussion

The main features presenting in these cases are summarized in Table I.

It is apparent that the disease is diagnosed at an earlier age in pregnant women than in the general population. Undoubtedly in many cases pregnancy causes abnormal symptoms which may not otherwise develop for many years. In the case reported by Brugsch and Brodie (1948) diagnosis was made in a 26-year-old primigravida as a result of the investigation of a persistent severe urinary infection. The investi-

TABLE I

| Case | Age | Parity | Highest blood-pressure | Size of kidneys | Remarks |
|---|---|---|---|---|---|
| *1* | 26 | 2 | 250/170 | Grossly enlarged | Death at 33/52 uraemia |
| *2* | 25 | 2 | 170/120 | Grossly enlarged | Eclampsia in 1st pregnancy. Urinary infection. |
| *3* | 33 | 1 | 140/90 | Moderately enlarged | Recurrent urinary infection. |
| *4* | 26 | 1 | 240/150 | Grossly enlarged | Urinary infection and haematuria. Mild accidental haemorrhage. |
| *5* | 42 | 8 | 110/74 | Moderately enlarged | Large polycystic liver. |

gation of a similar complication led to the diagnosis in Case 3 of the present series.

Three of the 5 cases developed recurrent urinary infection during their pregnancies, but response to chemotherapy and/or antibiotics was good and the infection did not present a serious problem. In 10 of the 11 cases reviewed by Crabtree (1942) pyelonephritis was regarded as severe, and in 1, pregnancy was terminated on account of resistance to treatment. The increased dilatation of the already distorted and enlarged renal pelves, together with the pressure of the growing uterus on the enlarged kidneys, almost certainly increases urinary stasis and favours severe urinary infection. With a wide range of antibiotics at our disposal today, urinary infection is easily controlled in the majority of cases; and it is most unlikely that pregnancy would require to be interrupted on this account.

Hypertension was severe in 3 cases (1, 2, and 4), absent so far in Case 5, and developed to a mild degree in the last month of pregnancy in Case 3. It was the most serious complication encountered and led in 1 case to renal failure and death from uraemia. Eclampsia had occurred in a previous pregnancy in Case 2, and Callaghan (1950) describes a case of fatal eclampsia occurring in a patient aged 26 years with grossly enlarged polycystic kidneys.

The degree of hypertension largely depends on the size of the kidneys. In the 3 cases with severe hypertension, the kidneys were grossly enlarged and, of the cases reviewed in the literature, severe hypertension was invariably associated with a gross degree of polycystic kidneys. Conversely, moderately enlarged kidneys are rarely associated with hypertension, in the absence of other disease.

If hypertension is present in the earlier months of pregnancy in patients with polycystic disease, the outlook is poor. Almost invariably the hypertension becomes progressively worse as pregnancy advances. Initially, the development of the hypertension is associated with an interstitial nephritis resulting from the ischaemia caused by the pressure of the cysts on the vascular tree of the kidney. The pressure of the enlarged uterus may interfere further with the blood supply to the remaining cortical tissue and increase the degree of interstitial nephritis that is already present, thereby establishing a vicious circle which may lead to irreparable kidney damage.

The development of a superimposed pre-eclampsia may also lead to rapid deterioration in cases where there is already considerable renal damage but, when the blood-pressure has been normal in early pregnancy, the occurrence of pre-eclampsia is not necessarily followed by a persistent hypertension, although it may favour the onset of hypertension at an earlier age than in the non-pregnant cases. In Case 2 eclampsia had occurred in her first pregnancy. In the puerperium, her blood-pressure fell to 110/70 and remained at that level until her dismissal from hospital, but by the second month of her next

pregnancy, the blood-pressure was 170/120 and did not return to normal after termination of the pregnancy.

In general, hypertension is one of the commonest complications of pregnancy, and although most frequently associated with pre-eclampsia, or of the "essential" type, the possibility of a urinary tract abnormality which might cause it must not be overlooked. Silbernagel (1952) has quoted the following urinary tract abnormalities which may be responsible for the development of hypertension:

(1) Cysts of the kidney.
(2) Polycystic kidney disease.
(3) Obstructions of the urinary tract—ureteral strictures, twists, kinks or dilatation (congenital or acquired).
(4) Hydronephrosis and pyelonephritis.
(5) Phaeochromocytomas.
(6) Goldblatt's hypertension or renal ischaemia.

These abnormalities may be demonstrated by pyelography, and in the investigation of hypertension in pregnancy, particularly in the earlier months, the more frequent use of intravenous pyelograms would seem advisable. The discovery of unilateral urinary tract disease might provide an indication for nephrectomy or other surgical treatment, with improvement in the hypertension in many cases.

One patient in the series (Case 5) had had a succession of pregnancies without any complications. At no time had there been hypertension and the kidneys were not grossly enlarged.

There must be many women with minor degrees of undiagnosed polycystic disease of the kidneys who have gone through pregnancies without any complications developing which might have drawn attention to the disease.

The general consensus of opinion is that, in the absence of symptoms, pregnancy can safely be allowed to occur (Branham, 1947; Brugsch and Brodie, 1948; Findley, 1947; Crabtree, 1942; Gibson, 1952; Silbernagel, 1952).

Because of the hereditary tendency in polycystic disease, which may be transmitted through either sex, and because the disease is incurable, the view is held by some that pregnancy should be discouraged. The risk of transmission does not, however, appear to be high, and patients anxious to have a family should be allowed to do so if they are fit enough, but they should be warned of the possibility of the disease in their offspring.

## Conclusions

The cases described above comprise only a small series, but from a study of these and the cases reported in the literature, the following conclusions seem justified:

(1) In the absence of abnormal signs or symptoms, polycystic disease of the kidneys is no contra-indication to the continuation of the pregnancy.

(2) Urinary infection is frequent, but nowadays can usually be satisfactorily controlled by chemotherapy or antibiotics, and pregnancy should be allowed to continue.

(3) In the presence of hypertension the continuation of pregnancy is a hazardous procedure and interruption is advised.

I wish to express my sincere thanks to Dr. John Hewitt and Mr. W. S. Mack for their advice and help.

## References

Bourland, J. W. (1946): *Urol. cutan. Rev.*, **50**, 669.
Branham, J. (1947): *J. Urol., Balt.*, **57**, 519.
Brugsch, H. G., and Brodie, S. (1948): *Bull. New Engl. med. Cent.*, **10**, 208.
Callaghan, E. T. (1950): *New York J. Med.*, **50**, 2309.
Cannon, J. F. (1947): *Ann. intern. Med.*, **27**, 610.
Crabtree, E. G. (1942): *Urological diseases of pregnancy*. Little, Brown & Co., Boston. Pp. 293 and 360.
Crawford, R. H. (1933): *Surg. Gynec. Obstet.*, **36**, 185.
Findley, P. (1947): *J. Mt Sinai Hosp.*, **14**, 293.
Gibson, T. E. (1952): *Amer. J. Obstet. Gynec.*, **63**, 1326.
Morris, N. (1952): *J. Obstet. Gynaec. Brit. Emp.*, **59**, 822.
Rall, J. E., and Odel, H. M. (1949): *Amer. J. med. Sci.*, **218**, 399.
Silbernagel, W. M. (1952): *J. int. Coll. Surg.*, **17**, 96.

# A STUDY OF EFFECTS OF X-RAYS ON THE GRANDCHILDREN OF WOMEN WHO HAVE BEEN IRRADIATED FOR THE TREATMENT OF FEMALE STERILITY*

BY

IRA I. KAPLAN, B.Sc., M.D., F.A.C.R.

*Clinical Professor Radiology, N.Y.U.-Bellevue Medical Center*
*Director Emeritus, Radiation Therapy Dept., Bellevue Hospital,*
*New York, N.Y.*

FROM generation to generation the physician has sought newer and better methods of combating female sterility, and has seized upon every new discovery with optimistic hopes.

It was the discovery of Halberstadter, in 1905, that X-rays had a specific action on the ovaries and the observations of Béclère (1909) and others that led to the use of irradiation to alleviate female sterility, especially in such cases where every other known therapeutic measure had been tried and failed. Today it is readily and generally recognized that low dosage X-ray therapy is a proper and effective method for the treatment of female infertility.

In 1950, before the 5th International Congress of Radiology, I presented a report covering an experience of 25 years of such therapeutic administration of X-rays. In this report I noted the successful relief achieved in cases with the production of normal children and also, more important, the birth of grandchildren to the originally irradiated sterile female. It must be realized that one is required to wait a long period of time in order to note the appearance of these third generation grandchildren, a period of about 20 years, and that has been required of me in this work. Today I am ready to report upon the successful birth of quite an appreciable number of normal grandchildren whom I have been able to trace and who were born to children of women originally irradiated for sterility 20 or more years ago (Kaplan, 1928).

In my opinion, the treatment of human female infertility with X-ray therapy would have been more universally accepted were it not for the pronouncements of possible dire genetic effects to follow such treatment, especially those prognosticated by Muller (1950), based upon experiments with *Drosophila*.

The observations of the normal grandchildren which I am herein reporting, representing third generation follow-ups on women who received irradiation for sterility, substantiates my oft-repeated assurance that normal children of irradiated mothers may expect to subsequently produce normal offspring, that is grandchildren to the originally irradiated infertile female.

Rubin (1952), in a recent report on "Third Generation Follow-up in Women Receiving Pelvic Irradiation", states, "the long span of time between generations obviously makes it difficult to give an absolute answer to the theoretical question of the ultimate harmful genetic effects of irradiation on the human race. But the long interval of time between births of a first and second generation would warrant the assumption that whatever harmful effects may have been produced by the X-ray irradiation to the ovaries of a grandmother would have been dissipated over the years."

Israel (1952), in an address before the American Gynecological Society, presented his observations in an appreciable number of cases of women treated by irradiation for sterility. Israel stated, "the challenge is to recognize that dosage which is genetically harmless." He stated also, "proper selection of patients and fixed low dosage assure the method's immediate safety. Late genetic sequelae have been imputed to low

*Presented before the 7th International Congress of Radiology in Copenhagen, Denmark, July 1953.

dosage ovarian irradiation because of certain observations in animals. Recent studies, however, show that experimental data may not be relied upon to predict the occurence of induced genetic changes in man. This thesis is supported by the fact that the quantity of X-rays administered to animals has been not only too long in comparison to the quantity administered in low dosage therapy but also has been of the whole body type. The latter technique makes it particularly difficult to collate experimental observations and clinical results."

Unfortunately, most of the adverse criticism of the use of irradiation in the relief of female sterility is based upon the genetic observations made on animal experimentation. While it is known that one can demonstrate genetic abnormalities in lower animals following irradiation, however, as Wolf (1950) stated, there is no substantial evidence of such changes occurring following X-ray therapy to the ovaries in human beings. Mazer and Israel (1951) recently stated that "no one has reported adverse effects on the patient and her immediate offspring." Muller's dire prognostications in 1950 regarding the evil genetic effects likely to occur in women treated by X-rays were based solely on his experimental work mainly with the *Drosophila* fly.

In human X-ray therapy, as used for the treatment of female sterility, the X-rays are readily confined to the limited area for which treatment is designed. There is no doubt that this fact plays an important role in the harmlessness of therapeutic irradiation as used in the treatment of human female sterility.

While it has been ascertained experimentally that certain effects of irradiation upon the reproductive organs of some insect species can be observed in their subsequent successive generations, Haldane (1947) and Glücksmann (1947) believe that we are not justified in extrapolating such effects to human beings. On this question of comparing the effects of irradiation on the *Drosophila* and the effects of irradiation on the human infertile female, Rubin has this to say: "Irradiation of the *Drosophila* produces its lethal effects by direct action from within a few minutes to hours after fertilization. The eggs are collected in batches, deposited on food provided for that purpose, and are irradiated shortly after they are laid. Even if the insect is irradiated, the action is almost the same, as the tissues overlying the gonads afford them little protection.

"Apart from other incomparable biologic and constitutional differences between the two species, the immediate irradiation effects on the human female's ovaries are essentially dissimilar because of their anatomic structure and position in relation to the overlying tissues. The dose to each human ovary as applied in the treatment of recurrent amenorrhoea and infertility is about 175 r. According to D. E. Lea (1947), the 50 per cent dose for a batch of *Drosophila* eggs irradiated within 30 minutes of laying, when usually not more than one or two nuclear divisions have occurred, is 290 r. This dose for the fly's eggs can prove to be lethal and has no validity for women.

"It is well known that young women can recover ovarian function, become pregnant, and give birth to normal children, after receiving a castration dose of X-ray.

"There is a vast difference between the action of X-rays in early pregnancy and its action when applied to intact ovaries in non-pregnant women. This possibly also accounts for the general confusion concerning the mutational effects that result from low dosage X-ray irradiation of dysfunctioning ovaries in cases of habitually delayed menstruation.

"There is another basic biologic difference between irradiating *Drosophila* eggs and the ovaries of non-pregnant women, namely, in the reproductive cycles. The *Drosophila* reproduces itself in about 10 days, some 30 generations being produced within one year, although its life cycle is about 90 days. After irradiation, little time is left between generations for full recovery from its effects to take place. In contrast to secondary effects on progeny of the *Drosophila*, an interval of at least 20 years elapses between generations in populations of western countries."

The following case histories amply illustrate third generation follow-up in women who received pelvic irradiation for the relief of female sterility over 20 years ago. These successful

results give evidence that whatever damage may have been done to the reproductive organs of these sterile women was temporary and had left no permanent effect on the genes of their subsequent second and third generation progeny.

The histories of these cases are herewith described in detail.

Mrs. C. A., aged 28, was referred on 9th June, 1925, for amenorrhoea, dysmenorrhoea and sterility. Menstruation began at 11 years and was never regular. She married at 26 years of age and continued to have irregular, painful periods and was unable to conceive. Her last period was on 3rd May, 1925. The husband was tested and found to be potent. Previous therapy had proven of no avail and X-ray therapy was recommended.

She received a course of X-ray therapy to the ovaries in the prescribed manner between 9th June and 30th June, 1925. Following treatment, the patient menstruated regularly for 9 months without pain, became pregnant, and on 21st December, 1926, gave birth to a normal baby girl.

This baby girl matured normally, menstruated regularly, beginning at the age of 13. She was married on 4th March, 1946, at the age of 20. Contraceptives were used for one year. Then she became pregnant and on 22nd October, 1948, gave birth to a perfectly normal baby boy, weighing 6 pounds at birth. She continued to function normally, again conceived, and on 13th October, 1950, gave birth to a normal baby girl.

Mrs. M. M., aged 24, was referred on 22nd February, 1927, for X-ray treatment for sterility. Her menstruation began at 12½ years of age, and was always irregular, with periods occurring at 2—3 months intervals. She married at 21 years of age and after 2 years of marriage, not becoming pregnant, she sought medical advice. A curettage was performed but this and subsequent glandular medication therapy failed to alleviate the sterility. Her last menstruation occurred in March 1926, 11 months prior to X-ray therapy. X-ray therapy was administered in the usual manner between 22nd February and 7th March, 1927, to the ovaries and pituitary.

She responded well to the treatment, menstruated and became pregnant and gave birth to a normal baby boy on 18th November, 1928, a girl on 28th August, 1930, another girl on 8th August, 1934, and a fourth child, a girl, on 18th July, 1940.

The boy born on 18th November, 1928, developed normally and served in the United States army during the second World War. In 1949, he married, and his wife readily conceived, and on 10th March, 1950, gave birth to a normal baby boy, weighing 8 pounds, 3½ ounces. In 1951 she again conceived, and on 26th October, 1951, she bore a baby girl. Both children are perfectly normal.

The oldest daughter of Mrs. M. M., born 30th August, 1930, was married on 20th January, 1952, promptly became pregnant without difficulty, and on 20th August, 1952, gave birth to normal twins, a boy and girl, thus illustrating the normalcy and fertility of these children born to an irradiated sterile mother.

On 26th September, 1952, the second daughter of Mrs. M. M., born in August 1934, was married but as yet has not desired pregnancy.

Mrs. H. B., aged 22, was referred for irregular menstruation and sterility on 12th March, 1925. She menstruated at 13½ years of age, always irregularly. She married at 21 years and shortly after became pregnant, but miscarried at one month of gestation in August 1924. She again menstruated in October 1924 and again in January 1925. Failing to conceive, and other forms of therapy proving unavailing, she was referred for X-ray therapy. Treatment was given only to the ovaries, on 12th and 19th March, 1925. She responded well to the treatment, menstruated in April 1925, became pregnant, and on 16th January, 1926, was delivered of a normal baby girl. This girl developed normally, menstruated regularly at 13, and married in March 1949. She readily conceived and gave birth to a normal baby boy on 30th August, 1950. In 1953 she again conceived and is due to give birth to another child in November 1953. Thus she will have produced 2 grandchildren to Mrs. H. B.

Mrs. L. K., aged 31, was referred on 18th March, 1926, for irregular menstruation and sterility. Her menstruation which was always irregular began at the age of 14 and her last period occurred on 31st December, 1925. She married at the age of 29 and continuing to be irregular and not conceiving she sought medical aid. There was no anatomical abnormality and the tubes were patent. Medication proving unavailing, she was referred for X-ray therapy. Treatment was administered to the ovaries. She responded well and in June 1926 conceived, and on 20th March 1927, gave birth to a normal baby boy. She continued to menstruate regularly and again conceived, and on 28th June, 1929, gave birth to a second normal baby boy. In 1932 she again conceived but, because of persistent pernicious vomiting and distress, she was therapeutically aborted.

The older son, born on 20th March, 1929, grew normally, matured well, and married in 1950. On 24th September, 1951, his wife gave birth to a normal baby boy, this being a grandchild of the originally irradiated sterile female (L. K.).

The second son is normal, is at present in the army and is engaged to be married.

Mrs. M. B., aged 24, was referred for irregular menstruation and sterility on 10th October, 1927. Her menstruation began late, at 16 years of age, and was always irregular with periods occurring at 3—4 months intervals. Her last period was on 4th July, 1927. She married at the age of 22 and continued to function

without any change in the menstrual cycle. Not conceiving she sought medical attention which proved unavailing. She was then referred for X-ray therapy. Treatment was administered only to the ovaries. She responded well and menstruated regularly until she became pregnant in December 1927. On 18th August, 1928, she gave birth to a normal baby girl. She subsequently became pregnant twice again but terminated the pregnancies by self-induced abortion both times, May 1929 and January 1936.

The girl born in August 1928 matured and functioned normally and on 22nd November, 1950, married a young officer on active duty in the United States navy. Conception was avoided until February 1953 when she readily conceived and had a normal baby girl on 15th October, 1953.

The following case is of interest because it illustrates that a second child born of an irradiated sterile mother can also mature, marry, conceive and bear normal third generation children.

Mrs. L. S., aged 33, was referred for amenorrhoea and sterility on 13th January, 1925. Her menstruation began at 18 years of age and was always irregular. Interestingly, she was married at the age of 17 years and 11 months, and menstruation appeared a month after marriage, and there was bleeeding at each intercourse. Three years later, at the age of 21, having not conceived, she sought medical attention. Curettage was recommended and carried out in 1923. No menstruation occcurred during the following year, in spite of medication, and then it appeared irregularly. The last two periods, before X-ray therapy, occurred on 17th October, 1924, and 25th December, 1924. X-ray therapy was administered to the right and left anterior and posterior ovarian areas and to the right and left thyroid areas between 12th and 30th January, 1925. She responded well to treatment and menstruated regularly March to June 1925 and then became pregnant. On 19th March, 1926, she gave birth to a normal baby boy. She continued to menstruate normally and again conceived, and on 7th March, 1928, gave birth to a normal baby girl. She continued to menstruate normally but avoided conception for a year, then conceived again, and on 13th April, 1930, gave birth to a baby boy. All these children were normal and grew well and matured. The daughter, second child of Mrs. L. S. menstruated normally at puberty and on 19th November, 1949, at the age of 21, married and continued to function normally, readily conceived in June 1950 and on 29th March, 1951, gave birth to a normal baby girl, a granddaughter to the irrrdiated mother, Mrs. L. S. She continued to menstruate normally, conceived again and on 11th February, 1952, gave birth to a second child, a normal boy, that is a second grandchild to Mrs. L. S. The oldest son of Mrs. L. S., born on 19th March, 1927, was married on 29th October, 1951. As yet, however, his wife has not desired conception.

Mrs. E. R., aged 22, was referred on 10th October, 1928, for treatment of amenorrhoea and sterility. The menarche appeared at the age of 12½ years and periods were always irregular. She married at 19 years of age, continued to have irregular periods, gradually became stouter and failed to conceive. The last period occurred on 26th September, 1928. She was referred for X-ray therapy after all other forms of treatment proved unavailing. Irradiation was administered to the ovaries and pituitary on 10th, 16th, 23rd October, 1928. She responded well, conceived and on 30th August, 1929, gave birth to a normal baby girl. She continued to function normally and on 2nd August, 1931, gave birth to a baby boy and on 4th February, 1936, to a baby girl. The first girl, born on 30th August, 1929, grew, matured normally and on 23rd September, 1951, married. She readily conceived and on 23rd September, 1952, gave birth to a normal baby boy, 7 pounds 4 ounces, a grandson of the originally treated Mrs. E. R.

Mrs. F. C., aged 30, was referred on 14th October, 1927, for scanty menstruation and sterility. She was a large, very obese woman. The menarche appeared at 14 years of age, and menstruation, while regular, was always scanty. She married at the age of 22 and, failing to conceive, sought medical attention. She became pregnant late in 1925, and in August 1926 was delivered of a full-time stillborn baby. Menstruation was scanty and the last period occurred on 22nd September, 1927, and lasted scarcely one day. She was then referred for X-ray therapy. This was administered only to the ovaries on 14th and 27th October, 1927. She responded well and menstruated regularly, then conceived in May 1930, and on 18th March, 1931, was delivered of a normal baby boy by Caesarean section. In 1933 she died of intercurrent disease.

The boy grew, developed normally, enlisted in the Marines and was married on 6th January, 1951. His wife readily became pregnant and gave birth to a normal baby boy on 1st March, 1953, a grandchild of the originally treated Mrs. F. C.

Mrs. M. Mc., aged 25, was referred for irregular menstruation and sterility on 21st February, 1927. Her menstruation began at 13 years of age and was always irregular. Her last period was on 6th December, 1926. She married at 21 years of age and continued to be irregular. After several years of treatment by several gynaecologists she was referred for X-ray therapy. Treatment was administered only to the ovaries. She responded well to the X-rays and menstruated normally. She, however, deferred trying to conceive until March 1930. On 31st January, 1931, she gave birth to a normal baby girl. She continued to menstruate regularly but developed hypertension

and was advised by her physician not to have any further pregnancies.

The girl, born in January 1931, matured normally menstruated regularly since puberty and married in November 1951. She became pregnant shortly thereafter, and on 6th September, 1952, gave birth to a normal baby boy.

The following case histories represent the follow-up of women who were irradiated for sterility, who responded to irradiation and bore normal children. These children have married, but as yet have not produced children, that is, grandchildren of their originally irradiated mothers.

Mrs. I. G., aged 30, was referred for lack of menstruation on 17th September, 1926. She had started menstruating at 12 years of age and was regular until the age of 22, when she became irregular with periods of intramenstrual bleedings. She married at the age of 27, and immediately became pregnant, but miscarried in September 1924. She resumed menstruation but was always irregular. There was no period between February and July 1925, and she was then curetted, but menstruation did not apear until October 1925, and ceased again until 16th May, 1926, when it appeared rather scantily. She was referred in September 1926 for X-ray therapy since all other treatments had not helped. X-ray therapy was administered between 17th and 27th September, 1926, to the ovaries and the pituitary. Following X-ray treatment she menstruated 4 times normally then became pregnant, and on 10th November, 1927, gave birth to normal twin girls. She continued to function normally, and on 14th September, 1930, gave birth to a normal baby boy. The twin girls matured normally, and on 27th October, 1951, one was married. Because of economic conditions, however, she has not as yet wished to become pregnant. The son born on 10th November, 1927, married while in the army and was soon thereafter sent to Korea, but evidently had impregnated his wife before he left. Returning in August 1952, finding his wife had been unfaithful and that she had been aborted, he divorced her.

The following represents the history of another case of recent marriage of the daughter of an irradiated mother.

Mrs. M. U., aged 28, was referred for treatment of irregular menstruation and sterility on 12th August, 1927. The menarche appeared at 13 years of age and menstruation was always irregular, occurring about every 3 months. The last period occurred on 13th May, 1927. She married at the age of 20, and the menstruation continued to be irregular. She sought medical attention but did not conceive. In 1925 a curettage was carried out but no relief followed. Patency tests were satisfactory. She was referred for X-ray therapy and this was administered only to the ovaries on 12th, 23rd, 30th August, 1927. She responded well, menstruated and immediately conceived, and on 24th March, 1928, gave birth to a normal baby girl. This girl matured and functioned normally, became engaged in 1950, but after a few months this was broken. On 22nd November, 1952, she was married to a dentist. She is as yet not pregnant.

Mrs. S. E., aged 24, was referred on 22nd October, 1924, for treatment of irregular menstruation and sterility. Her menstruation began at the age of 13, was regular for a short period then persistently irregular up to the time of treatment. The last period had occurred on 4th October, 1923. She married at the age of 21, used no contraceptives but failed after 3 years of marriage to conceive, in spite of medications and tubal patency tests. X-ray therapy was advised and administered to the ovaries and the pituitary on 22nd, 28th October, 4th November, 2nd December, 1924. She responded well, conceived, and on 15th October, 1925, gave birth to a normal baby boy. She continued to menstruate normally, conceived again and on 25th April, 1927, gave birth to a second normal boy. The older boy born in 1925 developed well, served in the army during World War II, then entered medical school, graduated in 1952, began his internship in a well-known hospital, and on 9th November, 1952, married. His wife is now (November 1953) in the fifth month of pregnancy. The second son is still at college.

Mrs. M. R., aged 28, was referred on 31st July, 1930, for sterility of 6 years' duration. Following X-ray therapy she conceived, and on 17th July, 1931, gave birth to a normal boy. She continued to function normally and on 28th November, 1934, she gave birth to a second boy.

The first boy, born in 1931, married in December 1952, and has moved to California. I have not as yet been notified about any offspring.

In the following cases the children of irradiated mothers are now engaged but not as yet married.

Mrs. B. C., aged 26, was referred on 27th October, 1927, for X-ray therapy for amenorrhoea and sterility. She menstruated at 12½ years of age and was always irregular. The last period occurred in September 1926, and the one previously in September 1925. She received medical care and had been regularly taking prescribed hormone pills without favourable effect. She married at 21 years of age and continued to be irregular, and continued medication. Exploratory operation and a curettage were recommended and carried out early in 1925, without any favourable effect, and menstruation only occurred twice since then, September 1925 and September 1926. She was then referred for X-ray therapy which was adminis-

tered only to the ovaries on 27th October and 2nd November, 1927. She responded well, menstruated regularly for 3 months thereafter, became pregnant, and on 27th November, 1928, gave birth to a normal baby boy. The boy, now 24 years of age, is normal and healthy in every way and is now engaged to be married, which is planned for October 1953.

Mrs A. G., aged 27, was referred on 27th October, 1929, for treatment of irregular menstruation and sterility. Her menstruation began late, at the age of 17, and was always irregular, occurring at 3-months intervals with pain. She was always obese. She married at the age of 24 and used no contraceptives but did not conceive. The last period occurred on 16th July, 1929. Medical treatment proving of no avail, X-ray therapy was suggested and administered to the ovaries and pituitary on 27th September, 4th and 11th October, 1929. She responded well, conceived and on 25th August, 1930, gave birth to a baby girl, and continuing to function normally on 21st July, 1932, bore a normal baby boy. The girl grew and matured normally and is now (1952) engaged, but marriage awaits the return of her fiancé, who at present is on military service in Korea.

Of the 14 grandchildren already born, 9 are boys and 5 are girls. There is one set of twins, a boy and girl. Based, therefore, on this study, I feel properly justified in stating that X-ray irradiation when properly applied for the treatment of amenorrhoea and sterility in human females is harmless both to the mother and to the child born to such an irradiated woman and also to the subsequent grandchildren.

In no way can the abnormal genetic effects found in the offspring of irradiated animals be extrapolated to human beings.

(The photographs of these grandchildren, presented in lantern slides, shows the normal appearance of these grandchildren.)

As for the grandchildren so far born, all of them have been carefully examined by competent paediatricians and have been found normal in all respects. The grandchildren of Mrs. H. A. are children of a practising paediatrician.

## Conclusion

Of a large group of married females treated for irradiation, 252 successfully responded and bore 293 normal children. Eighteen of these children born 20 or more years ago, have already married and produced 14 normal living children, that is third generation grandchildren of the originally irradiated sterile women. Of this group, 9 are boys and 4 are girls, and among these there is one set of twins. Two of these second generation women are at present pregnant. The grandchildren are normal in all respects.

As a result of this study it may properly be said that irradiation when properly administered for female sterility is harmless to the mother, her children and subsequent grandchildren.

## References

Béclère, A. (1909): *Arch. Roentg. Ray.*, **14**, 142.
Glücksmann, A. M. (1947): *Brit. J. Radiol., Suppl.*, **1**, 101.
Halberstadter, L. (1905): *Klin. Wschr.*, **42**, 64.
Haldane, J. B. S. (1947): *Brit. J. Radiol., Suppl.*, **1**, 99.
Israel, S. L. (1952): *Amer. J. Obstet. Gynec.*, **64**, 971.
Kaplan, I. I. (1928): *Amer. J. Obstet. Gynec.*, **15**, 658.
Kaplan, I. I. (1950): *J. Obstet. Gynaec. Brit. Emp.*, **57**, 767.
Lea, D. E. (1947): *Action of radiation on living cells.* Macmillan, New York.
Mazer, C., and Israel, S. L. (1951): *Menstrual disorders and sterility.* 3rd edition. Hoeber, New York.
Muller, H. J. (1950): *Amer. Scient.*, **38**, 33.
Roland, M., and Weinberg, A. (1951): *Amer. J. Obstet. Gynec.*, **62**, 1167.
Rubin, I. C. (1952): *J. Amer. med. Ass.*, **150**, 207.
Wolf, S. (1950): *Amer. J. Obstet. Gynec.*, **59**, 259.

# OBSERVATIONS ON THE COMPOSITION OF TOTAL LEUCOCYTE COUNTS DURING THE HUMAN MENSTRUAL CYCLE

BY

I. L. MACKINNON, M.B., Ch.B.

*Senior Lecturer in Anatomy*
*University of London King's College*

MACKINNON (1949) demonstrated a characteristic pattern in leucocyte counts during the menstrual cycles of a group of women, but was unable to obtain statistically "significant" results for any one woman.

Subsequently blood samples were obtained (MacKinnon, 1953) under basal conditions, from a healthy woman, aged 25, during 13 menstrual cycles, and they showed that her total leucocyte counts were "significantly" higher during the 22nd–24th days than during the 4th–6th days of the cycles. The present investigation is a study of differential leucocyte counts obtained during the same menstrual cycles with a view to deciding the part played by each type of leucocyte.

## METHODS

Immediately on waking each morning, between 7 a.m. and 8 a.m. during the course of a year, blood films were prepared from a pulp stab. The slide spreader technique was used. The donor was a healthy unmarried woman, aged 25, whose menstrual cycles lasted from 25 to 29 days with an average bleeding phase of 4 days. Staining was by Geimsa's method.

Three hundred leucocytes in each blood film were identified at oil immersion magnification, and the percentages of neutrophil cells, lymphocytes, monocytes, eosinophil cells and basophil cells calculated. Absolute numbers of each were then calculated from total leucocyte counts obtained from the same pulp stab (MacKinnon, 1953). With a view to acquiring information relating to variations in the age of the circulating neutrophil cells polynuclear counts were made on each blood film. The polynuclear count (Cook and Ponder, 1927) is the total number of nuclear lobes in the nuclei of 100 neutrophil cells.

Tables were constructed to display for each day of the period of observation the number of neutrophil cells (Table I), lymphocytes (Table III) and monocytes (Table IV) per c.mm. of blood, and the polynuclear counts of the neutrophil cells (Table II). In addition, each table contains the arithmetic means of the counts for each day and for each 3 successive days of the menstrual cycle, and the standard deviations from each. Blank spaces denote days on which, due to intercurrent infection or other cause, it was not desirable to take blood samples. Dashes indicate days which were outside the limits of the menstrual cycles.

Graphs of the arithmetic means of neutrophil cell counts (Fig. 1), lymphocyte counts (Fig. 3) and monocyte counts (Fig. 4), and of the arithmetic means of polynuclear counts (Fig. 2) for each day of the menstrual cycle were constructed in order to illustrate numerical trends.

The arithmetic means of neutrophil cell counts for each day, and for various groups of days, of the menstrual cycle were compared statistically. Any two means whose difference exceeded twice the standard error of their difference were regarded as "significantly" different (Hill, 1950). The same method of analysis was applied to the arithmetic means of lymphocyte counts, monocyte counts and polynuclear counts.

Tables of daily eosinophil and basophil cell counts were constructed on the same plan as those of the neutrophil cells, lymphocytes and monocytes. Exhaustive analysis of them failed to elicit any "significant" difference in cell counts during the menstrual cycle. The tables are, therefore, not reproduced.

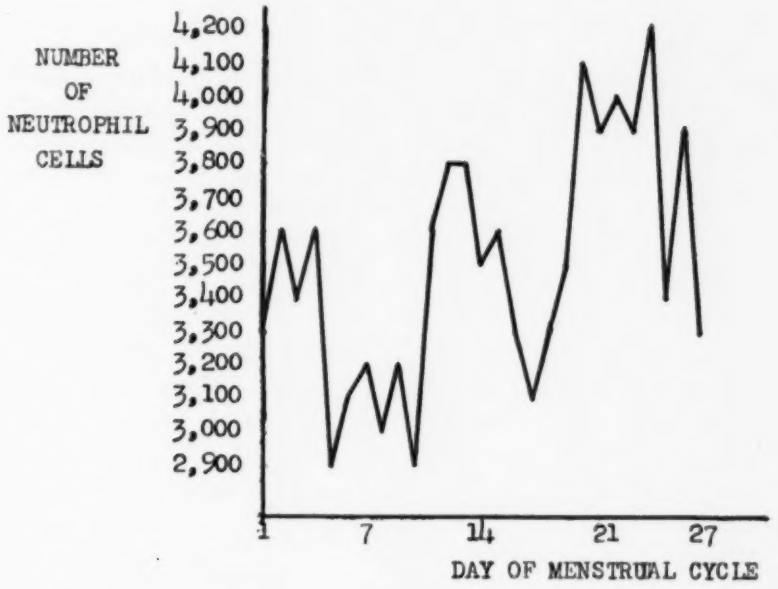



FIG. 1

Average number of neutrophil cells per c.mm. of blood for each day of the menstrual cycle.

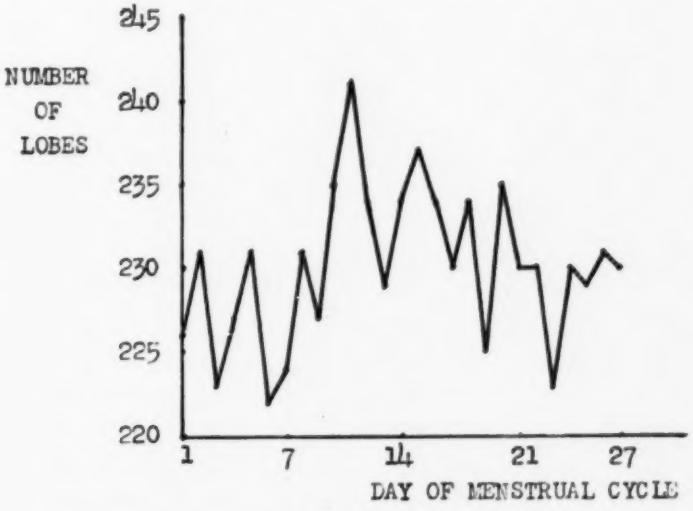



FIG. 2

Average polynuclear count for each day of the menstrual cycle.

## Results

Table I shows that the number of neutrophil cells circulating in the blood during the period of observation varied between a maximum of 6,800 per c.mm. and a minimum of 1,700 per c.mm. The average was calculated to be 3,490 per c.mm.

Neutrophil cell counts during the menstrual cycle (Fig. 1) were lowest from the 5th–10th days and highest from the 20th–24th days and, in addition, were high near the middle of the cycle, especially on the 12th and 13th days.

From statistical comparison (Hill, 1950) of the arithmetic means of neutrophil cell counts for single days and for groups of days during the menstrual cycle various " significant " relations emerge. For example, the counts of the 22nd–24th days are " significantly " higher than those of the 4th–6th days, the actual difference between their arithmetic means being 8 with a standard error of 2.76; and the counts of the 22nd–24th days are " significantly " higher than those of both the 7th–9th days and the 16th–18th days, the actual differences being 9 and 7.7 respectively and the standard errors 2.7 and 2.9 respectively.

The high neutrophil cell counts near the middle of the cycle with their maximum value at the 12th and 13th days just failed to prove " significantly " different from those on either side. For example, the actual difference between the arithmetic means of the 13th–15th day and the 7th–9th days is 5.3 with a standard error of 2.7 and the actual difference between the means of the 13th–15th days and the 16th–18th days is 6 with a standard error of 3.

Thus there is abundant evidence of " significant " differences between the low neutrophil counts of the follicular part of the menstrual cycle and the high neutrophil counts of the luteal part of the cycle, but the neutrophilia of the 12th and 13th days is not " significant ".

Table II shows that the polynuclear counts varied during the period of observation from 192 to 289. The average was calculated to be 231. Statistical comparison of the polynuclear counts during the menstrual cycle (Fig. 2) discloses that no " significant " difference exists between the counts for any 2 single days, or between the counts for any groups of 3 days. The average count of the 10th–18th days is, however, " significantly " higher than that of the 1st–8th days and the 19th–27th days, the actual differences being 7 and 5.6 respectively, and the standard errors 2.8 and 2.6 respectively. The age of the circulating neutrophil cells is, therefore, " significantly " greater during the central part of the cycle than during its earlier or later parts. The graph in Fig. 2 suggests that, following a sharp rise about the 10th or 11th day, the polynuclear counts fall gradually until about the 23rd day.

Table III shows that the daily lymphocyte counts obtained during the period of observation varied between a minimum of 800 per c.mm. and a maximum of 3,300 per c.mm. The average was calculated to be 1,776 per c.mm. During the menstrual cycle lymphocyte counts (Fig. 3) increased slowly until the terminal days of the cycle, when they fell. Statistical investigation discloses that the arithmetic mean of the 22nd–24th days is " significantly " higher than that of the 4th–6th days, the actual difference being 1.4 and the standard error 0.4; and that the arithmetic mean of the 14th–26th days is " significantly " greater than that of the 1st–13th days, the actual difference being 0.8 with a standard error of 0.035.

Table IV shows that the daily counts of monocytes circulating in the blood during the period of observation varied from a minimum of 46 per c.mm. to a maximum of 948 per c.mm. The average was calculated to be 348 per c.mm. Statistical comparison of monocyte counts during menstrual cycle (Fig. 4) elicits " significant " differences for the same groups of days as for the lymphocytes. Thus the actual difference between the arithmetic means of the 22nd–24th days and the 4th–6th days is 62 and the standard error 11.2; and the difference between the arithmetic means of the 14th–26th days and 1st–13th days is 63 with a standard error of 5.5.

The range of neutrophil cell counts during the menstrual cycle (Fig. 1) extends from a minimum of 2,900 per c.mm. to a maximum of 4,200 per c.mm. Precisely the same range is covered by the monocyte counts (Fig. 4) whose minimum number is 290 per c.mm. and whose maximum number is 420 per c.mm. The range of the lymphocyte counts (Fig. 3) is confined between

[Continued on page 885

TABLE I

*Neutrophil cell counts (in hundreds) for each day of 13 menstrual cycles, with standard deviations for each day, and for 3 successive days of the cycle*

| Day of menstrual cycle | Successive menstrual cycles | | | | | | | | | | | | | Average count for each day | S.D. for each day | Average count for 3 days | S.D. for 3 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | | | | |
| 1 | 22 | 37 | 30 | 21 | | 29 | 18 | 45 | | | 33 | 35 | | 33 | 15 | | |
| 2 | 41 | 25 | 28 | | | | 40 | 48 | | 36 | 33 | 34 | | 36 | 14.4 | 34 | 11.5 |
| 3 | 44 | 30 | 32 | | | 36 | 39 | | 48 | 24 | | 34 | 22 | 34 | 15.6 | | |
| 4 | 38 | 31 | | | | 37 | 31 | 31 | 42 | 26 | 68 | 32 | 23 | 36 | 17 | | |
| 5 | 32 | 23 | 38 | 30 | 38 | 22 | | 35 | 30 | 25 | 23 | 26 | 24 | 29 | 10 | 32 | 10 |
| 6 | 32 | 21 | 39 | | 35 | 25 | | | | 32 | | 31 | | 31 | 13 | | |
| 7 | 43 | 25 | 26 | 45 | | 20 | | | 35 | | 33 | | 30 | 32 | 15 | | |
| 8 | | 30 | | 35 | | 19 | | 21 | 42 | 40 | | 32 | 21 | 30 | 14 | 31 | 8.8 |
| 9 | 38 | 27 | 44 | 39 | | 34 | | 34 | 31 | | 22 | 27 | 22 | 32 | 12.4 | | |
| 10 | 20 | 25 | 37 | 30 | | | 18 | 33 | 35 | | 31 | 29 | 28 | 29 | 10.3 | | |
| 11 | 24 | 24 | 37 | 59 | | | 25 | 42 | 40 | 38 | 34 | 27 | 46 | 36 | 15.7 | 34 | 11.7 |
| 12 | | 30 | 36 | | | | 29 | 43 | 41 | 39 | 51 | 39 | | 38 | 17.3 | | |
| 13 | 38 | 31 | | 57 | | | 28 | | 39 | 37 | 40 | 36 | | 38 | 17.6 | | |
| 14 | 36 | 34 | 27 | 51 | | 34 | 38 | | 33 | 29 | | | | 35 | 15.9 | 36.3 | 11 |
| 15 | 34 | 30 | 31 | 48 | | 41 | 19 | 39 | 36 | | 42 | 38 | | 36 | 14 | | |
| 16 | | 23 | 32 | 39 | 41 | 22 | 31 | 45 | 34 | | 29 | 38 | | 33 | 14.4 | | |
| 17 | 24 | 22 | 31 | 34 | 30 | | 31 | 52 | 32 | | 26 | 32 | 30 | 31 | 13.7 | 32.3 | 11.1 |
| 18 | 22 | | | 36 | 29 | 25 | 58 | | 30 | 34 | 35 | 32 | 32 | 33 | 15.4 | | |
| 19 | | 29 | 30 | 32 | 30 | | | 34 | 35 | 27 | 43 | 38 | 55 | 35 | 15.1 | | |
| 20 | | 30 | 39 | 41 | 48 | 19 | 64 | 31 | | 44 | 49 | 43 | | 41 | 18 | 38.3 | 12.4 |
| 21 | 37 | 31 | 37 | 37 | 38 | 25 | 48 | 48 | 34 | | 55 | | 40 | 39 | 15.1 | | |
| 22 | 38 | 17 | 29 | 53 | 37 | 40 | 48 | 43 | 52 | 43 | 37 | 55 | 27 | 40 | 15.8 | | |
| 23 | 31 | 29 | 38 | 43 | 31 | 29 | 41 | 44 | 39 | 56 | 41 | | 50 | 39 | 15.4 | 40 | 12.2 |
| 24 | 28 | | 41 | | 41 | 50 | 48 | 57 | 35 | 34 | | 48 | 33 | 42 | 15.2 | | |
| 25 | 27 | | 38 | | 40 | 45 | 27 | | 22 | 31 | 35 | 31 | 39 | 34 | 12.3 | | |
| 26 | 30 | 37 | 32 | — | 48 | | 40 | 38 | 43 | 42 | 43 | 43 | 34 | 39 | 14 | 35 | 12.4 |
| 27 | 23 | 37 | 32 | — | 43 | 19 | 34 | — | | 32 | 46 | | | 33 | 15.8 | | |
| 28 | 21 | — | — | — | 33 | — | — | — | — | — | | | — | | | | |
| 29 | — | — | — | — | — | — | — | — | — | 42 | — | — | — | | | | |

TABLE II

*Polynuclear counts for each day of 13 menstrual cycles with standard deviation for each day and for 3 successive days of the cycle*

| Day of menstrual cycle | Successive menstrual cycles | | | | | | | | | | | | | Average nuclear count for each day | S.D. for each day | Average count for 3 days | S.D. for 3 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | | | | |
| 1 | 231 | 209 | 203 | 230 | | 212 | 258 | 257 | | | 227 | 211 | | 226 | 22.8 | | |
| 2 | 250 | 208 | 212 | | | | 271 | 232 | | 227 | 211 | 236 | | 231 | 24.5 | 226.1 | 21 |
| 3 | 202 | 227 | 226 | | | 218 | 237 | | 235 | 256 | | 203 | 217 | 223 | 21 | | |
| 4 | 197 | 203 | | | | 243 | 244 | 239 | 244 | 249 | 230 | 210 | 211 | 227 | 21.6 | | |
| 5 | 200 | 227 | 246 | 200 | 262 | 237 | | 243 | 234 | 242 | 241 | 216 | 219 | 231 | 20.2 | 227.4 | 20.5 |
| 6 | 196 | 240 | 204 | | 247 | 251 | | | | 216 | | 199 | | 222 | 31.8 | | |
| 7 | 226 | 232 | 213 | 207 | | 255 | | | 234 | | 217 | | 211 | 224 | 18.7 | | |
| 8 | | 218 | | 251 | | 243 | | 223 | 240 | 248 | | 215 | 210 | 231 | 20 | 227.3 | 16 |
| 9 | 229 | 208 | 239 | 234 | | 225 | | 251 | 215 | | 241 | 210 | 208 | 227 | 16 | | |
| 10 | 197 | 215 | 237 | 247 | | | 289 | 227 | 233 | | 236 | 231 | 239 | 235 | 26.4 | | |
| 11 | 223 | 245 | 223 | 241 | | | 276 | 269 | 233 | 244 | 247 | 223 | 225 | 241 | 22 | 237 | 21.1 |
| 12 | | 220 | 221 | | | | 266 | 245 | 242 | 239 | 236 | 206 | | 234 | 23.2 | | |
| 13 | 212 | 230 | | 227 | | | 216 | | 249 | 251 | 233 | 228 | | 229 | 19 | | |
| 14 | 250 | 219 | 210 | 208 | | 244 | 243 | | 256 | 245 | | | | 234 | 23.4 | 233.6 | 18 |
| 15 | 234 | 223 | 249 | 239 | | 255 | 254 | 220 | 240 | | 226 | 233 | | 237 | 18.2 | | |
| 16 | | 210 | 233 | 221 | 241 | 253 | 273 | 242 | 225 | | 235 | 211 | | 234 | 23 | | |
| 17 | 208 | 206 | 205 | 235 | 234 | | 255 | 241 | 242 | | 235 | 226 | 241 | 230 | 19 | 232.6 | 17.4 |
| 18 | 207 | | | 227 | 244 | 251 | 249 | | 236 | 236 | 240 | 220 | 230 | 234 | 17.7 | | |
| 19 | | 201 | 216 | 223 | 245 | | | 230 | 225 | 234 | 219 | 210 | 252 | 225 | 18.3 | | |
| 20 | | 228 | 209 | 245 | 249 | 279 | 231 | 225 | | 232 | 198 | 218 | | 235 | 19.5 | 230 | 17.8 |
| 21 | 235 | 216 | 233 | 232 | 221 | 270 | 235 | 229 | 226 | | 200 | | 241 | 230.7 | 19.4 | | |
| 22 | 248 | 213 | 219 | 224 | 223 | 244 | 254 | 237 | 224 | 227 | 221 | 221 | 237 | 230 | 15.7 | | |
| 23 | 216 | 224 | 221 | 224 | 220 | 241 | 240 | 219 | 210 | 217 | 220 | | 221 | 223 | 11 | 227.6 | 17 |
| 24 | 219 | | 248 | | 210 | 243 | 247 | 215 | 243 | 239 | | 212 | 231 | 230 | 19.5 | | |
| 25 | 209 | | 232 | | 235 | 251 | 270 | | 256 | 221 | 209 | 192 | 223 | 229 | 28.7 | | |
| 26 | 222 | 200 | 247 | — | 241 | | 244 | 238 | 233 | 223 | 221 | 212 | 261 | 231 | 20 | 230 | 21 |
| 27 | 233 | 221 | 235 | — | 222 | 258 | 225 | — | | 238 | 210 | | | 230 | 18.9 | | |
| 28 | 213 | — | — | — | 232 | — | — | — | — | | — | | — | | | | |
| 29 | — | — | — | — | — | — | — | — | — | 216 | — | — | — | | | | |

TABLE III

*Lymphocyte counts (in hundreds) for each day of 13 menstrual cycles, with standard deviations for each day, and for 3 successive days*

| Day of menstrual cycle | Successive menstrual cycles | | | | | | | | | | | | | Average count for each day | S.D. for each day | Average count for 3 days | S.D. for 3 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | | | | |
| 1 | 25 | 11 | 22 | 11 | | 12 | 21 | 16 | | | 19 | 14 | | 17 | 7.3 | | |
| 2 | 16 | 16 | 16 | | | | 17 | 22 | | 14 | 14 | 14 | | 16 | 7 | 17.0 | 1.7 |
| 3 | 25 | 13 | 18 | | | 18 | 23 | | 19 | 17 | | 17 | 11 | 18 | 7.3 | | |
| 4 | 28 | 16 | | | | 17 | 21 | 17 | 18 | 17 | 19 | 13 | 14 | 19 | 7.2 | | |
| 5 | 16 | 12 | 17 | 17 | 19 | 14 | | 17 | 12 | 16 | 11 | 16 | 8 | 14.6 | 5.3 | 16.7 | 5.5 |
| 6 | 27 | 13 | 14 | | 16 | 19 | | | | 16 | | 14 | | 17 | 8.4 | | |
| 7 | 24 | 13 | 16 | 22 | | 22 | | | 19 | | 16 | | 12 | 18 | 8.1 | | |
| 8 | | 15 | | 17 | | 19 | | 13 | 19 | 15 | | 16 | 16 | 16 | 7 | 17.4 | 6.1 |
| 9 | 33 | 12 | 20 | 21 | | 23 | | 16 | 14 | | 11 | 14 | 17 | 18 | 9.1 | | |
| 10 | 24 | 12 | 17 | 19 | | | 13 | 27 | 19 | | 13 | 16 | 18 | 18 | 7.1 | | |
| 11 | 14 | 9 | 13 | 15 | | | 17 | 18 | 16 | 19 | 20 | 20 | 23 | 17 | 5.9 | 17.3 | 5.0 |
| 12 | | 18 | 14 | | | | 14 | 13 | 16 | 23 | 23 | 17 | | 17 | 8.1 | | |
| 13 | 21 | 17 | | 23 | | | 16 | | 20 | 17 | 20 | 17 | | 19 | 7.2 | | |
| 14 | 19 | 17 | 9 | 31 | | 15 | 22 | | 12 | 15 | | | | 17 | 10.3 | 18.0 | 6.1 |
| 15 | 19 | 13 | 15 | 22 | | 14 | 19 | 17 | 18 | | 21 | 23 | | 18 | 7.1 | | |
| 16 | | 14 | 16 | 16 | 22 | 18 | 17 | 20 | 20 | | 23 | 14 | | 18 | 7 | | |
| 17 | 24 | 14 | 21 | 15 | 23 | | 20 | 22 | 23 | | 24 | 17 | 17 | 20 | 7.2 | 18.0 | 5.3 |
| 18 | 16 | | | 18 | 18 | 18 | 17 | | 18 | 13 | 17 | 14 | 14 | 16 | 6.5 | | |
| 19 | | 12 | 14 | 20 | 16 | | | 24 | 15 | 15 | 18 | 14 | 22 | 17 | 7 | | |
| 20 | | 20 | 20 | 14 | 19 | 12 | 23 | 15 | | 21 | 24 | 21 | | 19 | 7.2 | 19.0 | 4.9 |
| 21 | 22 | 22 | 22 | 17 | 23 | 27 | 19 | 19 | 13 | | 30 | — | 15 | 20 | 8.9 | | |
| 22 | 20 | 13 | 13 | 20 | 15 | 20 | 22 | 16 | 19 | 28 | 17 | 18 | 15 | 17.7 | 6.7 | | |
| 23 | 19 | 16 | 16 | 19 | 13 | 25 | 14 | 17 | 22 | 25 | 8 | | 15 | 17 | 8 | 18.1 | 5.6 |
| 24 | 22 | | 19 | | 17 | 26 | 19 | 22 | 14 | 14 | | 25 | 20 | 20 | 7.2 | | |
| 25 | 18 | | 17 | | 21 | 20 | 14 | | 14 | 17 | 16 | 17 | 16 | 17 | 6 | | |
| 26 | 16 | 12 | 12 | — | 21 | | 21 | 16 | 11 | 17 | 20 | 20 | 15 | 17 | 7.2 | 17.0 | 3.1 |
| 27 | 13 | 17 | 17 | — | 15 | 14 | 18 | — | | 19 | 18 | | | 16 | 6.2 | | |
| 28 | 13 | — | — | — | 21 | — | — | — | — | | — | | — | | | | |
| 29 | — | — | — | — | — | — | — | — | — | 14 | — | — | — | | | | |

TABLE IV

*Monocyte counts for each day of 13 menstrual cycles, with standard deviation for each day, and for 3 successive days*

| Day of menstrual cycle | Successive menstrual cycles | | | | | | | | | | | | | Average count for each day | S.D. for each day | Average count for 3 days | S.D. for 3 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | | | | |
| 1 | 306 | 260 | 275 | 175 | | 176 | 168 | 544 | | | 336 | 460 | | 300 | 302 | | |
| 2 | 308 | 276 | 230 | | | | 180 | 375 | | 330 | 378 | 255 | | 291 | 130 | 322 | 160 |
| 3 | 525 | 240 | 440 | | | 285 | 260 | | 592 | 315 | | 513 | 429 | 400 | 191 | | |
| 4 | 432 | 468 | | | | 290 | 165 | 385 | 396 | 322 | 360 | 450 | 336 | 360 | 150 | | |
| 5 | 260 | 222 | 480 | 371 | 650 | 200 | | 531 | 329 | 220 | 288 | 282 | 342 | 348 | 174 | 337 | 131 |
| 6 | 256 | 287 | 280 | | 265 | 288 | | | | 364 | | 343 | | 298 | 128 | | |
| 7 | 280 | 281 | 322 | 292 | | 135 | | | 420 | — | 212 | | 460 | 301 | 154 | | |
| 8 | | 243 | | 324 | | 120 | | 342 | 469 | 496 | | 380 | 697 | 384 | 227 | 333 | 150 |
| 9 | 546 | 210 | 340 | 390 | | 180 | | 270 | 188 | | 288 | 477 | 289 | 317 | 163 | | |
| 10 | 336 | 230 | 420 | 204 | | | 260 | 350 | 549 | | 450 | 360 | 350 | 351 | 157 | | |
| 11 | 160 | 273 | 448 | 312 | | | 230 | 195 | 594 | 504 | 232 | 294 | 791 | 367 | 221 | 340 | 149 |
| 12 | | 218 | 318 | | | | 240 | 300 | 384 | 320 | 234 | 306 | | 290 | 123 | | |
| 13 | 360 | 312 | | 246 | | | 46 | | 520 | 297 | 320 | 720 | | 362 | 254 | | |
| 14 | 350 | 385 | 234 | 448 | | 378 | 325 | | 254 | 441 | | | | 352 | 154 | 354 | 152 |
| 15 | 345 | 336 | 318 | 450 | | 180 | 152 | 490 | 505 | | 340 | 536 | | 350 | 169 | | |
| 16 | | 160 | 378 | 340 | 408 | 210 | 200 | 574 | 325 | | 336 | 399 | | 333 | 165 | | |
| 17 | 288 | 228 | 280 | 434 | 240 | | 335 | 350 | 320 | | 219 | 495 | 468 | 333 | 140 | 333 | 111 |
| 18 | 301 | | | 320 | 350 | 230 | 174 | | 340 | 416 | 378 | 357 | 440 | 331 | 131 | | |
| 19 | | 308 | 235 | 400 | 260 | | | 384 | 330 | 270 | 716 | 423 | 672 | 400 | 213 | | |
| 20 | | 456 | 320 | 420 | 360 | 72 | 475 | 300 | | 420 | 224 | 490 | | 348 | 187 | 374 | 197 |
| 21 | 400 | 200 | 272 | 420 | 128 | 176 | 504 | 948 | 350 | | 534 | | 225 | 400 | 226 | | |
| 22 | 420 | 279 | 322 | 574 | 220 | 210 | 385 | 455 | 486 | 525 | 416 | 640 | 490 | 418 | 176 | | |
| 23 | 330 | 282 | 420 | 630 | 245 | 496 | 480 | 402 | 480 | 534 | 265 | | 480 | 420 | 175 | 399 | 150 |
| 24 | 212 | | 350 | | 240 | 240 | 360 | 257 | 336 | 318 | | 756 | 420 | 349 | 164 | | |
| 25 | 240 | | 416 | | 325 | 225 | 318 | | 320 | 364 | 448 | 312 | 486 | 350 | 144 | | |
| 26 | 144 | 504 | 336 | — | 624 | | 395 | 360 | 365 | 528 | 408 | 378 | 400 | 404 | 186 | 364 | 132 |
| 27 | 234 | 318 | 495 | — | 441 | 102 | 275 | — | | 399 | 350 | | | 327 | 175 | | |
| 28 | 259 | — | — | — | 406 | — | — | — | — | | — | | — | | | | |
| 29 | — | — | — | — | — | — | — | — | — | 295 | — | — | — | | | | |

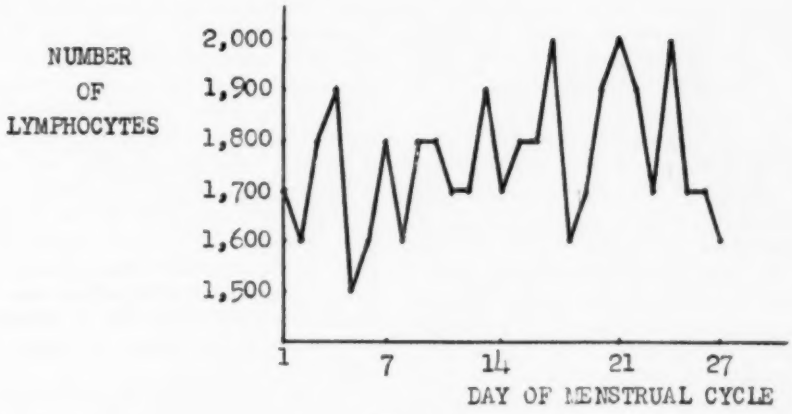



FIG. 3

Average number of lymphocytes per c.mm. of blood for each day of the menstrual cycle.

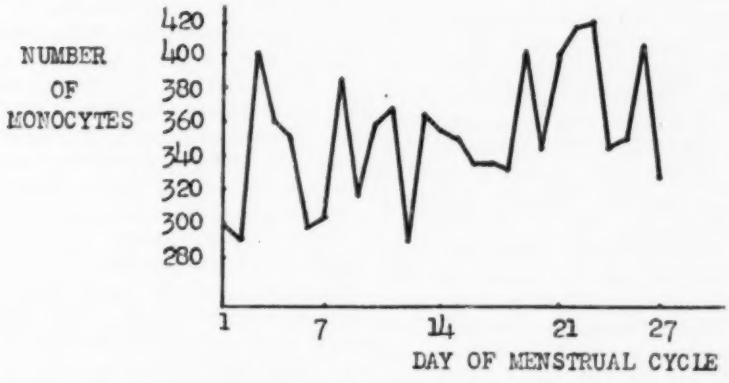



FIG. 4

Average number of monocytes per c.mm. of blood for each day of the menstrual cycle.

a minimum of 1,500 per c.mm. and a maximum of 2,000 per c.mm. The lymphocytosis of the luteal phase of the menstrual cycle is, therefore, less than the contemporary neutrophilia and monocytosis.

## DISCUSSION

The average leucocyte counts obtained during the present investigation were: neutrophil cells 3,490 per c.mm., lymphocytes 1,776 per c.mm., and monocytes 348 per c.mm. Wintrobe (1951) states that the average counts are: neutrophil cells 4,000 per c.mm., lymphocytes 2,100 per c.mm., and monocytes 375 per c.mm., but his figures are based on an average total leucocyte count of 7,000 per c.mm., whereas the present figures are based on a total count of 5,300 c.mm. The reason for the present counts being lower than Wintrobe's is that they were obtained under basal conditions (MacKinnon, 1953).

When adjustment is made for the difference in total counts the differential counts of the present investigation are of the same numerical order as those of Wintrobe, and can be regarded as normal.

The average polynuclear count of 231 obtained during this investigation is below the accepted average of 270 (Cook and Ponder, 1927). Haden's (1946) criterion for normality in nuclear pattern is that, in any blood film, the commonest number of nuclear lobes per neutrophil cell shall be 2 or 3. Out of the 265 films examined during this investigation 232 averaged 2 lobes and the remaining 33 films averaged 3 lobes. The nuclear configuration is, therefore, within normal limits. To ensure that the method of counting was uniform 40 films chosen at random were recounted. The results were almost identical with the original counts. All the counts were made by the author.

During the 4th–6th days and 22nd–24th days of the menstrual cycle polynuclear counts (Fig. 2) are of the same numerical order. During the latter group of days neutrophil cell counts (Fig. 1) are, however, " significantly " higher. Therefore, if it can be assumed that the length of life of neutrophil cells remains fairly constant during the menstrual cycle, the rate of their production must be higher during the 22nd–24th days than during the 4th–6th days. This would agree with the finding of Pai and Hsueh (1938) that young forms of neutrophil cells are commonest just after the middle of the luteal phase of the menstrual cycle. During pregnancy neutrophil cell counts are increased in the blood (Cason and Phillips, 1947) and their myelocytic precursors are increased in the bone marrow (Daniachij, 1936). It would therefore seem that the high neutrophil cell counts of the luteal phase of the menstrual cycle depend on increased production by the bone marrow in preparation for pregnancy.

The neutrophilia observed near the middle of the menstrual cycle (Fig. 1) appears to be coincident with ovulation which, during the period under review, occurred on the 11th–13th days of the cycle (MacKinnon, 1953). Polynuclear counts on these days (Fig. 2) indicate that the neutrophil cells are older than at any other time during the cycle. Therefore, the neutrophilia is not due to increased production of cells, but to the introduction of older cells into the circulation. Vasodilation, by releasing the cells from sequestration in closed capillaries (Vejlens, 1938) may be the cause. Vasodilation is one of the manifestations of oestrus, which is intimately concerned with ovulation, and which is almost ubiquitous among mammals, even including anthropoid apes (Corner, 1952). It is suggested that the ovulatory neutrophilia observed in the subject of this investigation resulted from mild vasodilation. Vasodilation could also account for the low body temperatures which are characteristic of ovulation.

The neurophilia (Fig. 1) demonstrated in this investigation during the luteal phase of the menstrual cycle was accompanied by a relative lymphocytopenia (Fig. 3). A similar leucocyte picture of neutrophilia with relative lymphocytopenia is characteristic of pregnancy (Andrews and Bonsnes, 1951), and can be obtained by injecting adrenocorticotrophic hormone (Hills, Forsham and Finch, 1948). Since the discovery by Venning (1946) that urinary corticoids are increased during pregnancy it can be assumed that adrenocorticotrophic activity is increased at that time, and may therefore be responsible for the leucocyte picture. The similarity of the leucocyte picture of the luteal phase of the menstrual cycle to that of pregnancy suggests that the production of adrenocorticotrophic hormone is increased during the luteal phase of the cycle and may be implicated, perhaps in co-operation with blood gonadotrophin (Wolf, 1939) and ovarian hormones (Young, 1950) in the production of the luteal leucocyte picture.

## Summary

(1) Counts of neutrophil cells, lymphocytes, monocytes, eosinophil cells, and basophil cells per c.mm. of blood, and of polynuclear counts, were obtained daily, under basal conditions, from the blood of one healthy unmarried woman, aged 25, during a period of a year incorporating 13 menstrual cycles.

(2) Neutrophil cell counts, lymphocyte counts, and monocyte counts were each shown to be " significantly " higher during the 22nd–24th

days than during the 4th–6th days of the menstrual cycle, and further "significant" differences were demonstrated between the high counts of the luteal phase and the low counts of the follicular phase in each case.

(3) No "significant" alterations in the eosinophil cell counts or in the basophil cell counts during the menstrual cycle were revealed by this investigation.

(4) The luteal neutrophilia demonstrated during the menstrual cycle was shown to depend on acceleration of the rate of production of neutrophil cells.

(5) A neutrophilia coincident with ovulation was observed, and was shown to depend on the introduction of mature cells into the circulation. Vasodilation was suggested as the cause.

(6) The lymphocytosis of the luteal phase of the menstrual cycle was shown to be less than the contemporary neutrophilia. It was argued that this is an indication of increased adrenocorticotrophic activity during the luteal phase of the cycle.

## References


Andrews, W. C., and Bonsnes, R. W. (1951): *Amer. J. Obstet. Gynec.*, **61**, 1129.

Cason, R. C., and Phillips, G. W. (1947): *Amer. J. clin. Path.*, **17**, 483.

Cook, W. E., and Ponder, E. (1927): *The polynuclear count.* Griffin, London. p. 7.

Corner, G. W. (1952): *Brit. med. J.*, **2**, 403.

Daniachij, M. A. (1936): *Zbl. Gynäk.*, **60**, 1220.

Haden, R. L. (1946): *Principles of hematology.* 3rd edition. Kimpton, London. p. 160.

Hill, A. B. (1950): *Principles of medical statistics.* 5th edition. Lancet Ltd., London. p. 243.

Hills, A. G., Forsham, P. H., and Finch, C. A. (1948): *Blood*, **3**, 755.

MacKinnon, I. L. (1949): *J. Obstet. Gynaec. Brit. Emp.*, **56**, 403.

MacKinnon, I. L. (1953): *J. Obstet. Gynaec. Brit. Emp.*, **60** (in press).

Pai, H. C., and Hsueh, C. S. (1938): *Chin. med. J.* (suppl.), 167.

Vejlens, G. (1938): *Acta path. microbiol. scand., Suppl.*, **33**, 1.

Venning, E. H. (1946): *Endocrinology*, **39**, 203.

Wintrobe, M. M. (1951): *Clinical hematology.* 3rd edition. Kimpton, London. p. 206.

Wolf, W. (1939): *Endocrinology in modern practice.* 2nd edition. Saunders, Philadelphia. p. 194.

Young, J. (1950): *Textbook of gynaecology.* 8th edition. Black, London. p. 61.

# THE MINOR DEGREE OF HYDROCEPHALUS AS AN OBSTETRICAL PROBLEM*

BY

T. FRANCIS REDMAN, M.B., F.R.C.S.E., M.R.C.O.G.
*Consultant Obstetrician and Gynaecologist, St. James's Hospital, Leeds*
*Formerly Lecturer in Obstetrics and Gynaecology, University of Bristol*

AND

G. R. AIRTH, M.B., D.M.R.(D.)
*Consultant Radiologist, Bristol Clinical Area*

THE fully developed hydrocephalic foetus presents an easy diagnostic problem once the condition is suspected: thereafter treatment follows a clear plan. A minor degree of hydrocephaly, however, may give rise to considerable clinical difficulty. The 3 cases to be described suggest that the problem is not quite as straightforward as textbooks would indicate.

CASE 1

*Hydrocephaly with no widening of sutures yet too large for vaginal delivery*

Mrs. J. J., a primigravida, 17 years old, was first seen at the antenatal clinic when 39 weeks pregnant. The baby presented by the breech. External version was performed after which the head remained high and could not be pushed into the brim, despite adequate pelvic size. It was thought that extension of the head might account for this but an X-ray was arranged in case there were some other abnormality. When the patient was seen 48 hours later the clinical position was unchanged but the X-ray department had reported the presence of a hydrocephalus, basing the decision on the relative sizes of pelvis and foetal head in the lateral view. (As the foetal head and the pelvic brim were in the same plane in this view, thereby eliminating distortion, this comparison should entail no fallacy.) In addition there was a spinal deformity in the lumbar region. On direct consultation the radiologist stated that he had no doubt about the diagnosis.

On the strength of this evidence, the patient was admitted to hospital and examined vaginally without anaesthesia preparatory to a proposed surgical induction of labour. It was realized that the finding of wide sutures would clinch the diagnosis and it was fully expected that the width of the sutures would leave no doubt in the mind of whoever examined the case. It was therefore with some surprise that no increased width of the sutures was felt.

Under general anaesthesia these findings were confirmed, the sagittal, lambdoidal and coronal sutures feeling quite normal, but in view of the strong radiological evidence and the fact that there was gross disproportion between the foetal head and the normal pelvis on head fitting, the hind waters were perforated.

At this stage the radiologist took further cephalometric pictures and then reported that they only confirmed his previous opinion. It was no longer possible to doubt that the foetus was abnormal, in fact, there was a clinical impression that the foetal head had increased in size while the case was under observation.

An inert labour ensued. When the cervix had dilated to admit three fingers the foetal skull was perforated and a great quantity of cerebrospinal fluid came away. The foetal head settled at once into the pelvis and the diagnosis was now satisfactorily confirmed. It was not possible to reach any sutures other than those mentioned above. Eventually an assisted delivery was effected under anaesthesia although the total labour had lasted 98 hours.

CASE 2

*Hydrocephaly of such minor degree that the diagnosis could not be made with certainty before delivery*

Mrs. G. F. was 38 years old and had had 2 previous normal vaginal deliveries, the largest baby weighing 8 pounds 2½ ounces. In the present pregnancy an antenatal examination at 36 weeks gestation revealed clinical cephalo-pelvic disproportion with a suspiciously large head as well as a contracted pelvis. X-ray cephalometry as well as pelvimetry was arranged (in the light of our experience with Case 1), and the report read as follows: "The foetal head is much too large for the brim but the brim is very small with an obstetrical conjugate of less than 3.75 inches. The occipito-frontal diameter of the foetal head measures 4.8 inches (12.2 cm.), this corresponds to the mean occipito-frontal diameter at 40 weeks, also to the upper limit of normal at 36 weeks. On these grounds hydrocephaly is not proven."

At 38 weeks gestation the patient was admitted to hospital as her blood-pressure had risen in 145/95. At 39 weeks the cephalometry was repeated, and this time the occipito-frontal diameter was 5.1 inches (13

* Read at a Meeting of the North of England Obstetrical and Gynaecological Society, held in Sheffield, on Friday, 17th April, 1953 (see page 945).

cm.), a value just within the normal maximum and about 1 cm. greater than the normal mean for 40 weeks gestation. These standards for the occipito-frontal measurements at various periods of gestation are taken from the graphs prepared by Hodges (1937).

In view of the disproportion and of the mild hypertension surgical induction of labour was planned. Under general anaesthesia a careful examination was made. The foetal head was very high and marked overlap was present. Through a tight cervix, which admitted only one finger with difficulty, fairly large fontanelles were felt but the cranial sutures were not wide enough to diagnose hydrocephaly with certainty, the widest showing only about ¼ inch separation. The conclusion was reached that the evidence was too equivocal to do anything but treat the foetus as normal.

After 5 days had elapsed labour failed to ensue, and, although there was no definite indication of intra-uterine sepsis, it was felt that lower segment Caesarean section should be performed, particularly as it seemed unlikely that so large a head (be it normal or abnormal) could pass so small a brim. The baby weighed 7 pounds 2 ounces and the measurements of its head taken after delivery were as follows:

(a) Occipito-frontal diameter ... 5¼ inches
(b) Biparietal diameter ... ... 4 inches
(c) Circumference ... ... 16 inches

The fontanelles were abnormally large but the sutures were no wider than can sometimes be felt in normal babies. However, the long circumference, the large fontanelles and the size of the head in relationship to the baby left little doubt that the infant was hydrocephalic.

CASE 3

*A hydrocephalic infant which had a normal vaginal delivery and was born alive*

Mrs. S. C., a primigravida, was 18 years old, and 5 feet tall. Her diagonal conjugate was estimated at 4¾ inches. Even at the onset of labour, 10 days after the expected date of confinement, the foetal head, presenting by the vertex, could not be made to engage in the pelvis. Some lack of flexion of the head existed but there was no gross overlap. During the 24 hours of labour 4 vaginal examinations were made; at no time did the obstetrician detect widened sutures. Eventually a normal delivery ensued with the help of an episiotomy. The baby had a gross lumbar spina bifida and bilateral talipes. Its head, which showed great moulding and elongation, was undoubtedly hydrocephalic with wide sutures and a large posterior fontanelle. The baby died 12 days after delivery.

## DISCUSSION

*How can closed cranial sutures in the presence of hydrocephalus be explained?*

It is to be expected with a minor degree of hydrocephalus that widening of the cranial sutures should not be very great. In such a case the compression of the foetal head during labour could be sufficient to close the sutures again, particularly if there is a meningocele to act as a reservoir for the cerebro-spinal fluid expelled from the cranium. That this is the likely explanation is shown by the third case described above: no abnormality of the sutures was detected during labour yet after delivery it was obvious that they were abnormally wide.

*How can minor degrees of hydrocephalus be diagnosed?*

Attention will first be directed to the condition by the presence of clinical cephalo-pelvic disproportion with a very high head which cannot be pushed down despite a normal-sized pelvic brim or merely by size of the foetal head on abdominal palpation. However, "head fitting" is not always as convincing as one would like, especially when there is soft tissue resistance to descent of the head; moreover, extension of the foetal head may give a false impression of abnormal size.

The clinician would next have recourse to the radiologist, hoping for incontrovertible proof of the existence of abnormality.

When eventually vaginal examination of the foetal head is possible, widely dilated sutures would clinch the diagnosis, but, as shown above, the clinician may occasionally be denied this confirmation of his opinion. As wide cranial sutures are always regarded as the *sine qua non* in the diagnosis of hydrocephalus the obstetrician may be excused if, in his perplexity, he turns once more to the radiologist in a somewhat doubting frame of mind. This occurred in Case 1.

One of us (G.R.A.) states: "An abnormally large foetal head shadow in an X-ray film, when this has been taken in an antero-posterior direction with the patient supine, does not necessarily denote hydrocephaly. So much is agreed amongst both obstetricians and radiologists, but when, from the film taken as above, there is suspicion of hydrocephaly, a lateral pelvimetry film should be made in addition; if the enlarged head is then seen in apposition to a brim of normal antero-posterior diameter, there is little reason to doubt that the enlargement is real.

When apparently normal sutures were felt through the cervix in this case, doubt was cast on the X-ray findings, in spite of evidence of a co-existent spinal abnormality; for this reason, confirmation was sought by cephalometry.

It would appear that obstetricians distrust measurements obtained by this means. Of the several available methods, I have found that of Cave (1943) both straightforward to perform and accurate in its results; two shadows of the foetal head are obtained on separate films, one being taken with the X-ray source relatively close to the patient, the second with the source removed as far as technical limitations permit; these two distances must be known accurately. The apparent measurement of the selected diameter is taken from each of the films, and calculation gives the actual measurement of that skull diameter.

Certain precautions must be taken:

1. The foetus must be encouraged to lie still by maternal overbreathing for a minute before the X-ray exposure, as in these cases the foetal head is often very mobile.

2. Cassettes must be changed and the X-ray tube moved to its new position quickly, to shorten the period between exposures.

3. The minimum distance of the X-ray tube from the film should be 30 inches; a lesser distance produces distortion and unsharp shadow, precluding accurate measurement.

4. The maximum distance should be 50 inches, to obtain adequate exposure of the film with apparatus currently available.

5. The X-ray source must be centred precisely over the foetal head.

It is found that, when the mother lies supine, the enlarged foetal head almost always presents as a true lateral view, but rotation of the sagittal plane 20° anteriorly or posteriorly from the true lateral produces very little change in the diameter presented for measurement. The occipito-frontal diameter, being precisely defined by bone, is preferable for measurement; the suboccipito-bregmatic and biparietal diameters are estimated from the calculated occipito-frontal.

The occipito-frontal diameter was found by Cave's technique in the present case to be 5.6 inches (14.2 cm.) and from this the biparietal was estimated as 4.3 inches (11cm.). From the radiological point of view, one might say that in this instance cephalometry was reassuring rather than necessary.

When hydrocephaly was suspected in Case 2 cephalometry was asked for immediately in the light of previous experience on Case 1, particularly as the reduced conjugata vera made direct comparison between foetal head and pelvic brim valueless. It is now apparent that a very minor degree of hydrocephalus can be present when the measurements of the foetal head are just within normal limits. At least it could be said that radiology enabled the obstetrician to have at his command as much evidence, with the exception of the circumference of the baby's head, as if the baby were already in his hands for measurement; one cannot ask for more.

It is felt that in clinically suspicious cases, where the measurements exceed those given in Hodges' graphs, hydrocephaly can be diagnosed with confidence.

It is not claimed that this degree of hydrocephalus, in which the sutures are closed, will be met with anything but rarely; it would be dangerous if hydrocephalus were diagnosed in these circumstances without the fullest consideration. It has not been possible to find specific mention of these borderline cases in literature or textbook, and the present report might be of assistance to anyone encountering such a case in the future.

*What should be the management of a case of minor hydrocephalus?*

Vaginal delivery of a small unperforated hydrocephalic head is not unduly rare, and the third case described above illustrates this. If there is real doubt in the diagnosis, allowing the labour to proceed is the only reasonable course. However, careful cephalometry in the hands of the expert may help to establish the diagnosis beyond reasonable doubt and perforation will improve the situation where easy vaginal delivery does not appear likely. Only when the obstetrician is faced with such a borderline hydocephalus as in Case 2 will cephalometry fail him, but if abnormality of the foetus is not clearly proven then Caesarean

section must be performed if the obstetrical situation would call for this line of treatment with a normal infant.

## Summary

1. Three case histories are presented, each illustrating some aspect of the problems in connection with minor degrees of hydrocephalus. The cases comprise:

(*a*) Hydrocephaly with no widening of cranial sutures during labour without perforation.

(*b*) Hydrocephaly of such minor degree that the diagnosis could not be made with certainty before delivery.

(*c*) A hydrocephalic infant which had a normal vaginal delivery without perforation and was born alive.

2. Three questions are posed for discussion:

(*a*) How can closed sutures in the presence of hydrocephalus be explained? It is suggested that the compression during labour may be sufficient to close the sutures, especially if there is a meningocele to act as a reservoir.

(*b*) How can minor degrees of hydrocephalus be diagnosed? Accurate and skilled cephalometry may be the deciding factor in diagnosis.

(*c*) What should be the management of a case of minor hydrocephalus? If doubt in the diagnosis exists labour should be allowed to proceed. Here again, radiography may be able to establish the diagnosis. If the obstetrical situation calls for Caesarean section, this must be performed as for a normal child unless the diagnosis of foetal abnormality is certain.

The help and advice given by Professor Lennon in the preparation of this paper is gratefully acknowledged. Our thanks also go to Mr. MacGregor, Senior Registrar, for his assistance in the management of the cases, and to Miss Dora Marston for the radiography.

## References

Bennett, M. D. (1953): Personal Communication.

Cave, P. (1943): *Brit med. J.*, **2**, 196.

Hodges, P. C. (1937): *Amer. J. Roentgenol*, **37**, 644.

# THE UTILIZATION OF RADIO-IODINE DURING PREGNANCY

BY

M. J. D. NOBLE, M.B., F.R.C.S.Ed., M.R.C.O.G.

AND

S. ROWLANDS, B.Sc., Ph.D., F.Inst.P.

*From the Departments of Obstetrics and Gynaecology and of Medical Physics at the University of Edinburgh; and the Clinical Research Laboratories of the Simpson Memorial Maternity Pavilion of the Royal Infirmary*

IT has been known for centuries that in many women there is some visible increase in the thyroid gland during pregnancy. Such enlargement of the gland has been recorded as occurring in from 60 to 80 per cent of pregnant patients specifically studied. Not a great deal is known of the histological changes occurring in the gland during pregnancy but apparently the increase in size is largely due to hyperplasia with perhaps the formation of some new follicles. Somewhat surprisingly, the increase in weight of the gland during pregnancy is unknown. The belief that there was an increased function of the gland in normal pregnancy led to the use of thyroid extract in the treatment of pre-eclampsia for it was noted that this condition did not usually develop in women whose thyroid glands enlarged during pregnancy (Nicholson, 1904). Certain phenomena occurring during pregnancy are similar to those of a mild hyperthyroid state. Thus the increased pulse pressure, mild tachycardia, warm extremities, functional cardiac murmurs, glycosuria and a tendency to " nervousness " are common to both conditions. However suggestive the clinical evidence may be that there is an increase in thyroid function during pregnancy, there is little specific evidence to support this.

## BASAL METABOLIC RATE

Sandiford and Wheeler (1924) pointed out that if the surface area of the foetus is added to that of the mother, the conventional methods of calculating the basal metabolic rate do not demonstrate any significant increase of the B.M.R. during pregnancy. Plass and Yoakam (1929), in a study of the basal metabolic rate in pregnancy, estimated that it increased from about +1 per cent at the end of the 3rd month of pregnancy to about +10 per cent at term. Hanna (1938) also found that there was an increase in the basal metabolic rate during pregnancy but came to the conclusion that, if the patients were really basal, both the normal and the highest pregnancy readings were within the range of ± 10 per cent. This was also Sontag's view (1944) in an excellent study of 158 pregnant women who had repeated estimations during pregnancy, for he found 72.9 per cent of his patients had a B.M.R. within the normal range at the 9th lunar month. He made the interesting observation that those women who had the lowest pre-pregnant levels generally had the greatest gain in pregnancy. There is, of course, no doubt that there is some rise in the basal metabolic rate in pregnancy but when the test is carried out on trained and intelligent patients the increase is perhaps not as great as is commonly thought.

## PROTEIN-BOUND IODINE (P.B.I.)

Man and her colleagues (1951) have investigated the protein-bound iodine levels in normal pregnant women. The normal level of this in non-pregnant women varies from 4 to 8 $\mu$g. per cent. In pregnancy the level increased from 6.2 to 11.2 $\mu$g. per cent with an average of 8.8 $\mu$g. per cent rising sharply from normal in the early weeks of pregnancy. The rise in the protein-bound iodine was not found to parallel that of the rise in the basal metabolic rate and a rise above normal occurred as early as the 6th week of pregnancy. This early rise in protein-bound iodine is somewhat puzzling and it is possible that substances other than thyroxine are being estimated. Man points out that a level of 11.2 $\mu$g. per cent of P.B.I. would in a non-pregnant individual be associated with a B.M.R. of 140 per cent. It was found that the protein-bound iodine

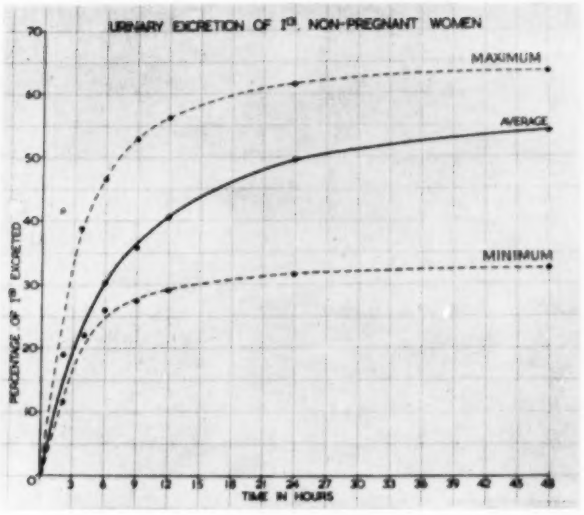



FIG. 1

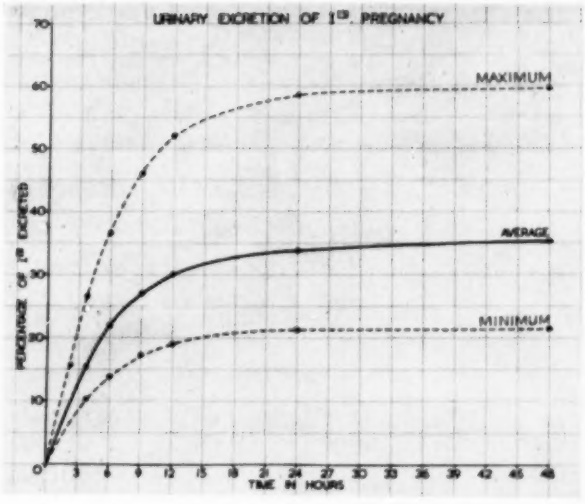



FIG. 2

M.J.D.N. & S.R.

was invariably raised in the last 24 weeks of normal pregnancy. De Mowbray and Tickner (1952) studied 41 healthy pregnant women between the 13th and the 40th weeks of pregnancy and found that in 22 (54 per cent) the protein-bound iodine exceeded 8 $\mu$g. per 100 ml. The average for the whole group was 8.8 $\mu$g. per 100 ml. and the range 4–20.

Probably the simplest method of testing thyroid function is to measure the urinary excretion of radio-iodine following the administration of a known amount. In this simple test the assumption is made that the amount of radio-iodine ingested is shared between the kidney and the thyroid, and thus the amount of radio-iodine excreted in the urine is that fraction of the dose which is not taken up by the thyroid. Myant (1952) has reviewed the problems associated with this method, the chief disadvantage of which is the overlap in different clinical groups. However, for the purpose of our preliminary work on radio-iodine excretion in pregnancy it was decided that the simplest method should be used.

## Methods

The method used has been described by Mason and Oliver (1949). The dose of radio-iodine administered was 10 microcuries and this was made up with a small quantity of carrier in the form of potassium iodide. The solution was given by mouth as a drink at 7 a.m., some half to three-quarters of an hour before breakfast. The bladder was emptied when the experiment commenced and a self-retaining catheter left *in situ*. Thereafter specimens were collected at 2-hourly intervals and then at 9, 12, 24 and 48 hours after the radio-iodine had been ingested. Ten ml. of urine from each sample were counted in a standard instrument and the total activity of the sample determined. This activity was expressed as a percentage of the standard solution, the results plotted and a graph drawn. Our patients were divided into three groups: (1) non-pregnant controls, (2) pregnant women who were more than 30 weeks advanced in their pregnancy, and (3) puerperal patients.

## Results

*Non-pregnant controls.* Twelve patients. These women were patients in the gynaecological wards and were restricted to women who had had or were about to undergo a minor gynaecological operation. Patients who had received iodine skin preparation were excluded. Fig. 1 shows the mean and the range of the results obtained. The mean percentage excretion at 24 hours was 47 per cent $\pm$ 14.2. Range: 32–62 per cent.

*Normal pregnant women.* Twenty-two pregnant women were studied and in all the pregnancy had proceeded beyond the 30th week. The mean percentage excretion at 24 hours was 32.9 per cent $\pm$ 10.25 within the range 21–60 per cent (Fig. 2). Two patients admitted for termination of pregnancy at the 16th week of pregnancy were studied. In one the 24-hour excretion was 58 per cent and in the other 60 per cent.

*Puerperal patients.* Twenty-five patients were studied at varying times between the 3rd and the 10th days of the puerperium. It was soon found that a simple urinary radio-iodine count could not be relied on as the breast milk was found to contain a varying quantity of radio-iodine. In 9 women the excretion of radio-iodine in the breast milk varied from 2 per cent to 21.8 per cent of the ingested dose with an average of 10.7 per cent. Honour, Myant and Rowlands (1953) noted that in two lactating women the clearance rate was 8.7 and 15.4 mil/min.—a figure approximating to that of the thyroid itself. The problem of radio-iodine excretion in the lactating woman clearly requires further study and will not be further discussed in this communication.

## Discussion

The urinary excretion of radio-iodine over the first 24 hours following its injection would appear to be approximately 50 per cent and in our own short series of non-pregnant women was 47 per cent. It is admitted, however, that the range is wide—28 per cent to 67 per cent in our patients, and 28 to 72 per cent in those of Mason and Oliver. These authors point out that, if the excretion from the 6th to the 24th hours is studied, the results are much more helpful in separating the various states of euthyroid and dysthyroid function. During these 18 hours the excretion of radio-iodine was between 10 and 15 per cent in their patients and the mean value in

our patients was 20 per cent. In thyrotoxic patients Mason and Oliver found that the mean radio-iodine excretion was usually under 4 per cent during this period.

The excretion of radio-iodine in our normal pregnant women was 32.9 per cent up to the 24th hour and the excretion between the 6th and the 24th hour was approximately 10 per cent. Thus the mean excretion of radio-iodine in the pregnant woman during this period lies between that of the normal non-pregnant woman, 20 per cent, and that of the thyrotoxic patient with a mean excretion of under 4 per cent.

These results would appear to indicate that there is an increased activity of the thyroid gland during the latter weeks of pregnancy. But it must be remembered that during this time the foetal thyroid is active and is presumably sharing in the increased iodine uptake of the mother. In fact, in a thriving infant the weight of the thyroid gland at birth is almost 10 per cent of that of its mother and could conceivably account for almost the whole of the increased maternal uptake. Clearly this point will require further investigation and the measurement of the difference between the radio-iodine content of the umbilical venous and arterial blood would provide data of immediate interest. In addition to the simple radio-iodine excretion tests that we have employed, clearance studies on the maternal thyroid gland are needed to enable us to apportion the role of the maternal or foetal thyroids in the utilization of the increased iodine uptake. Pochin (1953) has made the observation that in 5 pregnant women studied the radio-iodine uptake was slightly raised and that it was depressed during the weeks following delivery. No further comment on the raised protein-bound iodine values of pregnancy need be made here but it is obvious that there is some peculiarity in the high levels obtained in pregnancy and particularly in early pregnancy. Whether blood protein-bound iodine levels really represent the thyroid hormones in transit during pregnancy or not will require further study. The basal metabolic rate has obviously the most limited value in studying thyroid function in pregnancy and the modest increased values obtained in most cases are not very impressive. That the majority of the anterior pituitary hormones are being produced in increased quantities during pregnancy now appears probable but as yet nothing is known of thyrotrophic (T.S.H.) activity at this time.

In summarizing, therefore, all we can conclude from the available data and from the new facts presented in this paper is that it is highly probable that there is increased thyroid activity during pregnancy but as yet there are too many unknown factors to allow us to express this in any quantitative fashion.

## Summary

(1) The radio-iodine uptake in a series of non-pregnant, pregnant and lying-in women has been estimated.

(2) The radio-iodine uptake during the last 10 weeks of pregnancy is increased above normal by about 15 per cent.

(3) In 2 patients studied at the 16th week of pregnancy the radio-iodine uptake was within normal limits.

(4) In the lactating woman radio-iodine is excreted in the milk and in a series of 9 women 10 per cent of the dose of radio-iodine ingested by the mother was excreted in her milk.

This work was undertaken at the request of Professor Robert Kellar and we are indebted to him for much help. We are grateful to Sister Isdale of the University Department who was responsible for the supervision of the patients and the collection of samples. Part of the expenses was defrayed by the Barbour Watson Trust for Research in Gynaecology.

## References

De Mowbray, R. R., and Tickner, A. (1952): *Lancet*, **2**, 511.

Hanna, G. C. (1938): *Amer. J. Obstet. Gynec.*, **35**, 315.

Honour, A. H., Myant, N. B., and Rowlands, E. N. (1953): *Clin. Sci.*, **11**, 447.

Man, E. B., Heinemann, M., Johnson, C. E., Leary, D. C., and Peters, J. P. (1951): *J. clin. Invest.*, **30**, 137.

Mason, A. S., and Oliver, R. (1949): *Lancet*, **2**, 456.

Myant, N. B. (1952): *Brit. med. Bull.*, **8**, 141.

Nicholson, H. O. (1904): *J. Obstet. Gynaec. Brit. Emp.*, **5**, 32.

Plass, E. D., and Yoakam, W. A. (1929): *Amer. J. Obstet. Gynec.*, **18**, 556.

Pochin, E. E. (1953): *Clin. Sci.*, **11**, 441.

Sandiford, I., and Wheeler, T. (1924): *J. biol. Chem.*, **62**, 329

Sontag, L. W. (1944): *Amer. J. Obstet. Gynec.*, **48**, 315.

# PLACENTAL METASTASES FROM A BRONCHIAL CARCINOMA

BY

JAMES S. BARR, M.B., M.R.C.O.G.

*Senior Registrar, Department of Obstetrics*
*Stobhill Hospital, Glasgow*

THE subject of placental metastases from maternal malignant disease has received increasing attention (Bender, 1950; Cross, O'Connor and Holland, 1951) since it was reviewed by Holland (1949) when he presented details of a case unique in medical literature.

Varying types of malignant growth have been responsible for the features in the cases reported in the literature and these are summarized in Table I. The case now reported is apparently the first in which the primary tumour was a bronchial carcinoma.

## CASE HISTORY

The patient, a married woman aged 39, was admitted to the antenatal ward in November 1949 complaining of a troublesome cough and breathlessness. For some years she had been afflicted by chronic bronchitis and the present pregnancy, her seventh, had aggravated her symptoms. In addition to cough and dyspnoea she had for a few weeks prior to admission complained of pain in the right shoulder related to respiratory excursion. The date of her last menstrual period was 8th June, 1949.

It was obvious that her general condition was exceedingly poor. Dyspnoea was apparent as was a slight degree of cyanosis of lips and nail beds. In the chest there were widespread moist sounds throughout both lung fields and marked impairment of air entry in the right upper lung zone. A tentative diagnosis of pulmonary neoplasm was confirmed by the radiological findings.

The uterus was enlarged to the size of a 22-weeks pregnancy which was in accord with the period of amenorrhoea.

In consultation the physician and the thoracic surgeon agreed that the pulmonary lesion was too far advanced for operative interference.

Thereafter the patient's condition progressively deteriorated but, nevertheless, the pregnancy advanced and there arose the question of the advisability of terminating the pregnancy and of the place of palliative X-ray therapy. Both possibilities were rejected. Thus matters stood with a gradual decline in the patient's health until 2nd January, 1950, when slight vaginal bleeding occurred. This recurred at intervals for the next 2 weeks, at the end of which period labour commenced. This was short and terminated in the spontaneous delivery of a live 4-pound female child.

The placenta was expelled spontaneously and the greater part of it appeared normal although there was one pale pink friable area about the centre of the maternal surface.

TABLE I

| Author | Maternal disease | Placental metastases | Invasion of villi | Uterus affected | Child affected |
|---|---|---|---|---|---|
| Friedreich, 1866 | Carcinomatosis | Normal<br>No histology | — | Probably not | Yes |
| Berghinz, 1900 | Lympho-sarcomatosis | No report | — | Probably not | Yes |
| Walz, 1906 | Sarcoma of thigh | Yes | Yes | No postmortem | Craniotomy<br>no P.M. |
| Markus, 1910 | Melanotic sarcomata | Yes | Yes | No | No |
| Senge, 1912 | Carcinoma of stomach | Yes | Yes | No | No |
| Gray *et al.*, 1939 | Carcinoma of adrenal | Yes | Yes | Yes | No |
| Holland, 1949. | Melanoma of thigh | Yes | Probably yes | No | Yes |
| Bender, 1950 | Carcinoma of ethmoid | Yes | No | No postmortem | No |
| Bender, 1950 | Carcinoma of stomach | Yes | No | No | No |
| Cross *et al.*, 1951 | Carcinoma of breast | Yes | No | No | No |
| Barr, 1953 | Carcinoma of bronchus | Yes | No | No | No |

The patient survived the delivery and lived for a further 3 months, dying ultimately on 28th April, 1950. A postmortem examination revealed the following significant features:

A large bronchial tumour was present infiltrating extensively the right upper lobe of the lung and the corresponding bronchus. The tumour extended down the bronchial tree to involve the right middle and lower lobes. The pericardium was involved by direct spread. Metastases were found in the liver, pancreas, left suprarenal, left kidney and 4th lumbar vertebra. The left ovary was replaced by a tumour mass 7×4×2 cm. and a small tumour nodule was present in the other ovary.

*Histology*

The primary growth showed the general architecture and cell structure of a typical "oat cell" carcinoma, the cells being largely round or oval and containing little cytoplasm (Fig. 1).

In the placenta the suspiciously friable portions noted at delivery were revealed as old blood clot and fibrinous material. Examination of numerous sections eventually discovered a few small groups of abnormal cells in the maternal blood spaces. These were morphologically of the same type as found in the primary tumour. Figs. 2 and 3 are illustrative. The same type of malignant cells was demonstrated in the other sites of metastatic growth.

The infant made satisfactory progress and showed no evidence of tumour. She has now been observed and periodically examined for almost 3 years and continues to thrive. One may now assume that the child is unaffected by the maternal carcinoma.

## Comment

In this case, despite extensive spread of the tumour in the mother's tissues, the child escaped unharmed and it seems probable that this is the rule rather than the exception where pregnancy is complicated by maternal carcinoma. It appears that the placenta and more particularly the foetus do not easily become involved in metastases. On anatomical and physiological grounds it seems certain that malignant cells frequently reach the placental sinuses but rarely do they become established and multiply there. Table I reveals the infrequency of occurrence of invasion of the foetal villi and this is possibly associated with an active resistance on the part of the trophoblastic covering of the villus.

It may be that the presence of an active aggregation of malignant cells around a villus interferes with its nutrition and metabolism in such a manner as to produce atrophy and death of the cellular elements in the villus. The resulting stagnation and eventual cessation of circulation in the foetal vessels in the villus prevents embolic spread of malignant cells to the foetal tissues. That this is correct is supported by the observation in the present case that malignant cells were difficult to find in the placenta but where necrotic areas were present malignant cells could readily be demonstrated. A similar observation had previously been reported by Gray, Kenny, and Sharpey-Schafer (1939).

More recently Cross *et al.* (1951) have suggested that even should malignant cells reach the foetal tissues the environment might be unsuited for their continued existence and propagation.

The small number of reported cases which demonstrated foetal involvement lends some support to this view—in those of Friedreich (1866), Berghinz (1900), and Holland (1949) the primary maternal lesions were "carcinomatosis", lymphosarcoma and melanoma and these tumours are more commonly found in the very young than such growths as cancer of the breast, stomach, bronchus and cervix.

A further point of interest arose in the case recorded, namely, the clinical impression that the progress of the malignant disease was in no way accelerated by the presence of pregnancy. That indeed the reverse seemed to be the case was remarked on by the obstetrical and medical advisers alike. This is in accord with the widely held view that carcinoma in pregnant women does not advance rapidly on account of the pregnancy but rather follows a rate of progress typical of carcinoma occurring in an unusually young age group.

## Summary

A case of placental metastases from a bronchial carcinoma is described.

It is suggested that regular detailed examina-

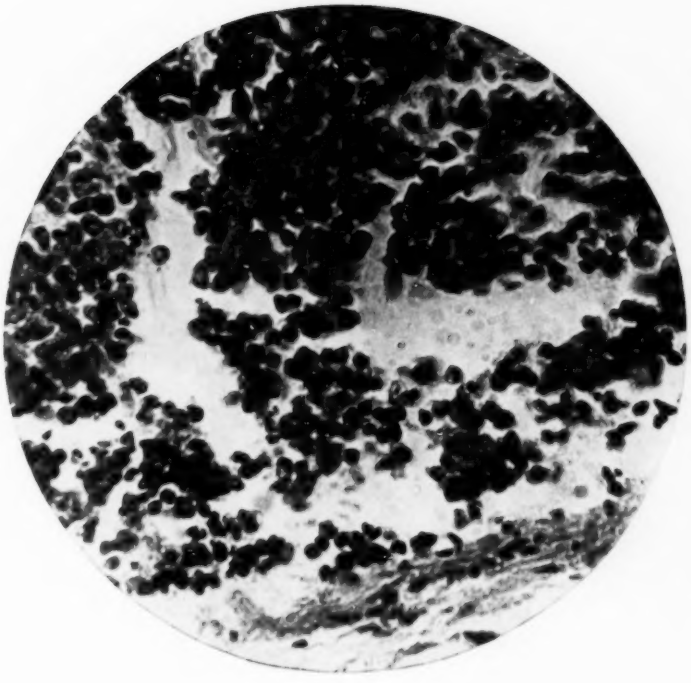


FIG. 1

Showing histological picture of primary tumour, revealing typical "oat cells" of a bronchial carcinoma. ×400

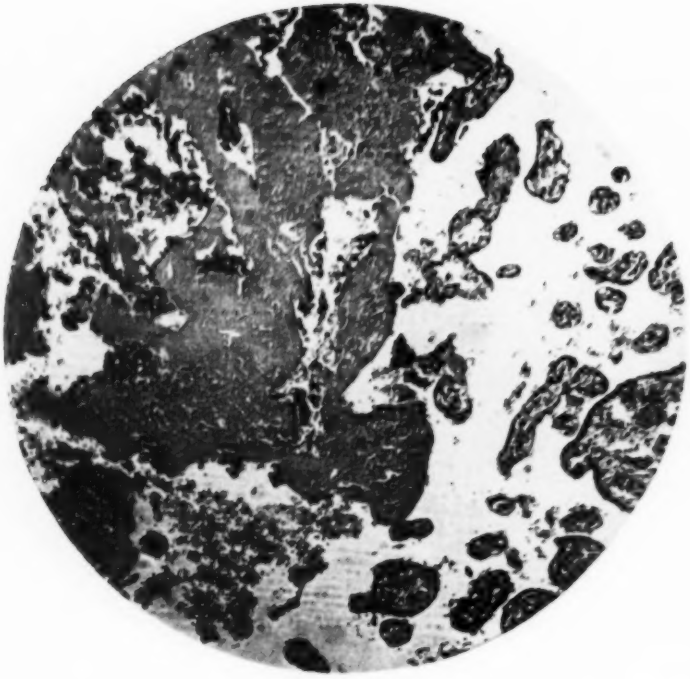


FIG. 2

Section of placenta, showing groups of deeply pigmented malignant cells among necrotic villi. ×100

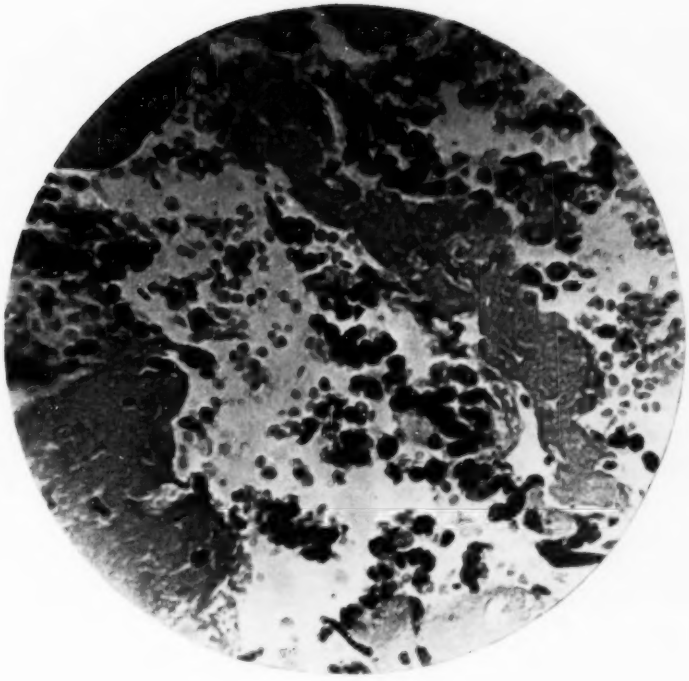


FIG. 3

Higher magnification of section of placenta shown in Fig. 2, and revealing groups of malignant cells. These cells should be compared with those seen in Fig. 1. ×400

tion of the placenta in cases of maternal malignant disease might reveal more cases of placental metastases.

Only by the study of sufficient reports will it be possible to hazard an opinion on the prognosis for the children resulting from pregnancies complicated by malignant disease.

I wish to express my thanks to Dr. Adam Barr for his guidance and for his suggestion that the placenta in this case should be subjected to a detailed examination. I am also grateful to Drs. Dick and McNaught of the Pathology Department for their histological examination of the placenta.

## References

Bender, S. (1950): *Brit. med. J.*, **1**, 980.

Berghinz, G. (1900): *Gaz. Ospedal. (Milan)*. (Quoted by Holland, E. (1949).)

Cross, R. G., O'Connor, M. H., and Holland, P. D. J. (1951): *J. Obstet. Gynaec. Brit. Emp.*, **58**, 810.

Friedreich N. (1866): *Virchows Arch.*, **36**, 465. (Quoted by Holland, E. (1949).)

Gray, J., Kenny, M., and Sharpey-Schafer, E. P. (1939): *J. Obstet. Gynaec. Brit. Emp.*, **46**, 8.

Holland, E. (1949): *J. Obstet. Gynaec. Brit. Emp.*, **56**, 529.

Markus, N. (1910): *Arch. Gynäk.*, **92**, 659. (Quoted by Holland, E. (1949).)

Senge, J. (1912): *Beitr. path. Anat.*, **53**, 532.

Walz (1906): *Verh. dtsch., path. Ges.*, **10**, 279. (Quoted by Holland, E. (1949).)

# CARCINOMA OF THE UTERINE BODY TREATED WITH RADIOACTIVE COBALT

BY

PAUL STRICKLAND, M.B., M.R.C.P., D.M.R., F.F.R.
*Assistant Radiotherapist, Mount Vernon Hospital, Northwood, Middlesex*

DURING 1950 supplies of radioactive cobalt ($CO^{60}$) became available from the Ministry of Supply Atomic Pile at Harwell, and we thought we might take advantage of this in evolving a simple irradiation technique in treating carcinoma of the uterine body. Radiocobalt has a half life of 5.3 years and emits gamma rays comparable to those of radium. It needs reactivating annually, having lost about 10 per cent of its activity.

Previous techniques have not proved entirely satisfactory. Many centres have used one or more radium tubes placed in the long axis of the uterus and left in position for 24 hours or longer. Because of screenage by the inactive ends of the tubes, the fundal portion of the uterus was probably under-irradiated. This is particularly important since a carcinoma may often take origin at the fundus, as is beautifully illustrated in Cullen's book (1900).

In recent years, Heyman, Reuterwall and Benner (1941) have described a "packing" method which apparently gives good results in their hands. However, elaborate apparatus is required, and the uterus has to be packed as tightly as possible with multiple radium tubes. There is an acknowledged risk of perforating the diseased uterus, and the method would not seem suitable for routine use.

We decided to design a flexible intra-uterine applicator containing multiple small sources of $CO^{60}$. Our criteria were that the apparatus should be simple to construct, easy to load and handle, and be capable of taking on accurately the pyriform shape of the cavity of the uterus after insertion. We aimed at a dose of irradiation of at least 6,000 röntgens at 1.0 cm. distant from the mucosal surface of the uterus in all directions. We decided to deliver this dose in two sessions of about 24 hours each, separated by an interval of one week—and this paper is a preliminary report of a trial of the method in a small group of cases.

*Description of Apparatus*

The apparatus consists of a tight spiral of stainless steel wire, resembling base clef piano wire. The length of loop to be used is determined by the passage of a uterine sound. When constituted, it is a springy appliance (labelled A in Fig. 1) and its open ends are pushed into two holes drilled in a brass cylinder (B) 2.0 cm. long and 1.95 cm. in diameter. The loop of wire thus formed is the container of the radioactive cobalt sources. It is closed by a brass plug and key (C).

With a little compression the loop can easily be passed through the "cervix tube" (D) which is a thin-walled brass tube of outside diameter 1.0 cm. The brass key fits snugly into a slot on the inferior surface of the cervix tube, at right angles to the plane of the loop.

*Method of Loading*

The flexible loop and cylinder are mounted on a small clamp and the cobalt sources are dropped into its open ends using long-handled forceps and working behind a thick lead screen. Each source is 2.0 mm. in diameter and is plated with nickel to absorb the soft beta radiation. The strength of each source is 2.8 millicuries and, in an average case, a total loading of 74 millicuries is used.

As each piece of cobalt is dropped in, an inert steel pellet follows so that the active sources are spaced equally round the loop, except at the

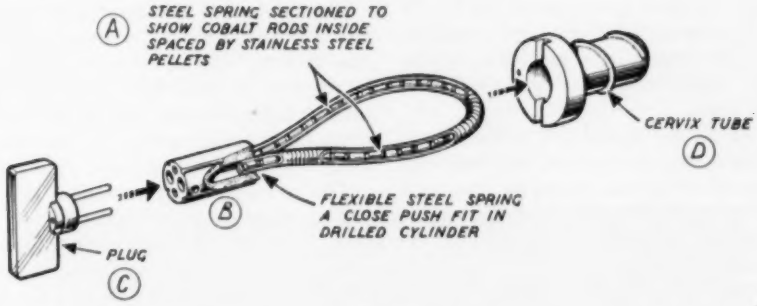



FIG. 1
Exploded diagram of applicator
*(Reproduced by courtesy of "Acta Radiologica")*

fundal region where 6 contiguous cobalt sources are used. The applicator is now closed by means of the plug and secured with a silk thread which passes through suitable holes in the cylinder and plug as shown in Fig. 1. The whole apparatus is now sterilized in the usual way.

A fuller description of the apparatus, with details of dose distribution around it has previously been published by Jones (1952).

*Method of Use*

Under general anaesthesia the patient is placed in the lithotomy position. Dilatation of the cervix is carried out, and a sound passed to determine the length of the uterus if this information is not already available. This is very important, for on it will depend the length of loop to be used. Gentle curettage is also performed to obtain material for histological study.

The anterior lip of the cervix is grasped gently with vulsellum forceps and drawn downwards. The cervix tube, on a solid metal introducer, is inserted, the introducer withdrawn and the tube remains in position. The distal end of the loop, with its attached cylinder, is now held in the right hand using modified tube-holding forceps. The cervix is steadied and the loop is gently fed through the cervix tube until it has disappeared from sight. The cylinder fits firmly into the cervix tube, and the key on the plug engages with the slot. The silk threads on the loop are twisted round a roll of flavine gauze and the vagina packed tightly. The whole operation lasts about 10 minutes.

The apparatus is left in position for 22½ hours, and is removed in the ward by simple traction on the silk threads. Removal is not unpleasant for the patient and anaesthesia is not required. The radiological appearance of the applicator in the uterus is shown in Fig. 2.

*Results*

Eight cases have been treated; all had been considered unsuitable for surgical treatment. The histology of the tumours was adenocarcinoma in all cases, of varying degrees of differentiation.

Of these cases, 5 are alive today and free of disease, the 2 longest survivors (our first 2 cases) having been treated 23 years ago. Our last case in this series was treated over 18 months ago and is well. The remaining cases have a variable follow-up between these two limits.

Three cases were unsuccessful: 1, treated in June, 1951, died in October 1952 with carcinomatosis. When first seen, she had a plaque of carcinoma half way down the anterior vaginal wall which was treated with a separate radium needle implant. Two other cases have died with widespread dissemination of disease. All 3 unfortunately died outside hospital and there was no opportunity for postmortem study.

## DISCUSSION

The mainstay of treatment of cancer of the uterine body is total hysterectomy, but there

exists a group of cases not suitable for it. In our series, the presence of severe cardiovascular disease or gross obesity have precluded operation in the opinion of the gynaecologists referring the cases.

It is now widely recognized that carcinoma of glandular origin may be just as radiosensitive as carcinoma of squamous origin as long as a sufficiently high dose of irradiation is given. This fact provides the rationale for an attempted radical radiotherapeutic technique.

Methods previously described are either too complex for routine use, or, because they employ central radium sources only, run a serious risk of underdosing the fundus uteri. If local recurrence of carcinoma occurs, it is most likely to occur there. By using an applicator moulded to the shape of the uterine cavity, and loading it differentially at its fundal end, we hope that this risk will be reduced. However, Paterson, Tod and Russell (1950), using a multiple radium tube technique, have reported that 72 out of 143 technically operable cases were clinically free of disease 5 years later, a crude survival rate of 50 per cent.

In several cases, curettage has been carried out after the completion of cobalt treatment. So far, no positive curettings have been obtained and this makes us confident that the disease can be eradicated locally. However, the method does not deal adequately with spread of disease into the parametria and, if such cases are accepted for treatment, supplementary deep X-ray therapy will be needed. Neither is a sufficient dose of gamma rays given to the upper third of the vagina, though the cervix itself is probably irradiated sufficiently.

The recurrence of cancer in the vaginal vault after hysterectomy is common, and is probably due to lymphatic permeation having occurred by the time of operation. In an attempt to deal with this, we intend in the future placing one or more radio-active sources in the vagina at the time of the insertion of the uterine applicator.

The morbidity of the method has been very slight. One or two patients have developed transient diarrhoea which has resolved uneventfully. It is likely to occur where the uterus is mobile and retroverted and the distance between applicator and bowel consequently diminished. The bladder has not been affected, and there have been no radiation necroses.

## Summary

A method of treatment of carcinoma of the body of the uterus, using a flexible applicator and multiple radio-active cobalt sources is described.

The work was carried out in close collaboration with Mr. D. E. A. Jones, Senior Physicist, Mount Vernon Hospital. I am grateful to the Gynaecologists for referring the cases, and to Professor B. W. Windeyer, and Dr. Roy Ward for encouragement and advice.

## References

Cullen, T. S. (1900): *Cancer of the uterus.* Kimpton, London.

Heyman, J., Reuterwall, O., and Benner, S. (1941): *Acta radiol., Stockh.*, **22**, 14.

Jones, D. E. A. (1952): *Acta. radiol., Stockh.*, **38**, 41.

Paterson, R., Tod, M., and Russell, M. (1950): *The results of radiotherapy, 1940–44, Manchester.* Livingstone, Edinburgh.

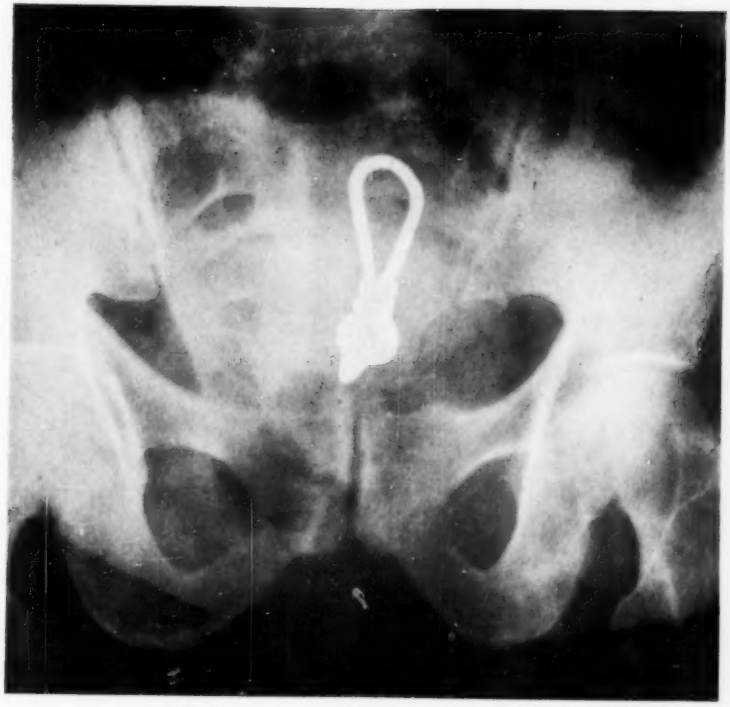


FIG. 2 (*a*)
Radiological appearance of applicator in treatment position
Antero-posterior view

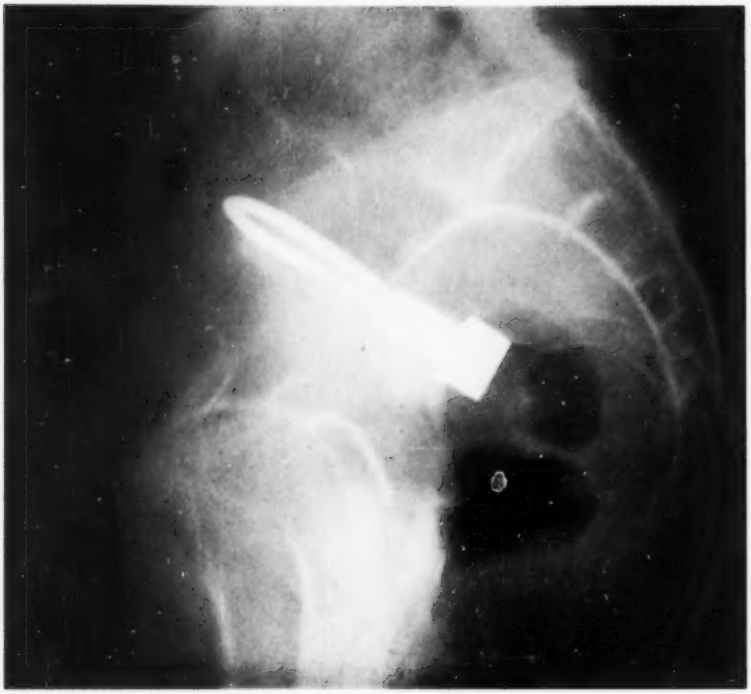


FIG. 2 (*b*)
Radiological appearance of applicator in treatment position
Lateral view

# THE COMPARISON OF THE PERINATAL MORTALITY RATES FOR A MATERNITY HOSPITAL

BY

JOHN THOMSON, M.D., D.P.H., D.C.H.

*From the Department of Child Life and Health, University of Edinburgh*

## INTRODUCTION

IN a recent publication (Thomson, 1952) it was noted that there had been a fall of approximately 50 per cent in the perinatal mortality rate of the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, when one compared the 2 years 1939–40 with the 4 years 1948–51. A decline of this magnitude invites explanation.

It is well known that the perinatal mortality rate of the non-booked portion of the population of a maternity hospital is much higher than the perinatal mortality rate of the booked portion of the same population. In consequence, because of the decline in the incidence of the non-booked portion of the population of the hospital from 21 per cent of the total hospital births for the 2 years 1939–40 to 12 per cent for the 4 years 1948–51, it has been suggested that this is the important cause of the decline in the perinatal mortality rate. This publication is an attempt to evaluate such a suggestion.

It has already been shown that the difference between the perinatal mortality rate of the booked group of cases and the non-booked group of cases in a maternity hospital is materially influenced by variation in the incidence of singletons and twins in the two groups as well as by variation in the incidence of low birth-weight infants (Thomson, 1952). These variable factors must also be considered in assessing the difference between the perinatal mortality rates for two different periods in the same hospital.

## METHOD

It is necessary to fix standard incidences for each of the factors to be investigated. The booking factor is arbitrarily standardized at an incidence of 9 booked infants for 1 non-booked infant.

The incidence of twins is standardized at 1 twin to every 39 singletons, this being approximately the incidence of twin pregnancies in the general population.

Birth weight incidence is arbitrarily standardized in a series of birth weight ranges as advocated in a previous publication (Thomson, 1952). These were, over 5½ pounds, 10; over 4 pounds to 5½ pounds incl., 0.5; over 2½ pounds to 4 pounds incl., 0.15; over 1 pound to 2½ pounds incl., 0.075. This distribution is probably not far removed from that pertaining to singletons in the general population.

The working method used is to ascertain the perinatal mortality rate per 1,000 total births for each of the birth weight ranges in respect of singletons and twins in booked and non-booked groups for each of the two periods under consideration. These perinatal mortality rates are then applied to the standardized incidence of birth weight ranges from which a standardized perinatal mortality rate per 1,000 total births for booked and non-booked singletons and twins for each of the two periods is obtained.

The next step is to ascertain the booked and non-booked perinatal mortality rate for each period when standardized for the incidence of twins. This is done by taking 39 times the standardized singleton perinatal mortality rate for booked and non-booked cases separately for each of the two periods plus in each case once the corresponding standardized twin perinatal mortality rate and dividing the total by 40.

Standardization for the incidence of booking is now done by taking, for each of the two periods separately, 9 times the standardized

booked singleton plus twin perinatal mortality rate plus once the standardized non-booked singleton plus twin perinatal mortality rate and dividing by 10.

## Results

In the 1939–40 period there were 5,353 births with 674 deaths and stillbirths giving an actual perinatal mortality rate of 129.1 per 1,000 total births. The corresponding figures for the 1948–51 period are 13,073, 949 and 72.6. This suggests that the perinatal mortality rate has been reduced by 43.8 per cent.

After standardization by the method suggested, the perinatal mortality rate per 1,000 total births for the first period becomes 80.44 and for the second period 55.25, a reduction in the mortality rate of 31.3 per cent.

Since the difference between the actual computation and the standardized computation is a measure of the inflationary effect of the varying incidence of singletons and twins, immature births, and booked and non-booked cases, it is clear that the major portion of the reduction in the perinatal mortality rate is not due to a combined action of these three factors.

Consideration of Table I shows that, with but 3 exceptions, every subgroup of singletons and twins in both booked and non-booked groups contributes towards the reduction in the perinatal mortality rate. The greatest saving of life has taken place in the booked singleton group over 5½ pounds birth weight, where there is a reduction of 39.8 per cent in the perinatal mortality rate. It is notable that the amount of the reduction of the perinatal mortality rate becomes less with a decline in the birth weight, until one reaches the smallest birth weight

Table I

*The perinatal mortality rate per 1000 total births in birth-weight groups of booked and non-booked cases*

| Birth-weight group | | Booked cases | | | | Non-booked cases | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Singletons | | Twins | | Singletons | | Twins | |
| | | 1939–40 | 1948–51 | 1939–40 | 1948–51 | 1939–40 | 1948–51 | 1939–40 | 1948–51 |
| Over 5½ pounds | Number | 3765 | 10309 | 56 | 184 | 833 | 1114 | 9 | 42 |
| | Perinatal mort. rate | 41.2 | 24.8 | 196.4 | 32.6 | 166.9 | 113.1 | 111.1 | 119.0 |
| Over 4 pounds to 5½ pounds | Number | 218 | 550 | 47 | 137 | 124 | 176 | 12 | 41 |
| | Perinatal mort. rate | 247.7 | 160.0 | 234.0 | 87.6 | 475.9 | 397.7 | 166.6 | 97.6 |
| Over 2½ pounds to 4 pounds | Number | 68 | 156 | 20 | 33 | 108 | 125 | 6 | 26 |
| | Perinatal mort. rate | 735.3 | 602.7 | 300 | 393.9 | 888.8 | 712.0 | 666.6 | 500.0 |
| Over 1 pound to 2½ pounds | Number | 31 | 89 | 9 | 14 | 42 | 62 | 5 | 15 |
| | Perinatal mort. rate | 1000 | 966.3 | 1000 | 928.6 | 976.2 | 967.7 | 1000 | 933.3 |
| All birth-weight Groups | Number | 4082 | 11104 | 132 | 368 | 1107 | 1477 | 32 | 124 |
| | Actual Perinatal mort. rate | 71.0 | 47.2 | 280.3 | 119.6 | 344.3 | 233.6 | 375.0 | 290.3 |
| Perinatal mortality rates corrected for birth-weight incidence | | 64.2 | 45.77 | 205.2 | 46.48 | 196.6 | 140.72 | 127.7 | 129.02 |

group where the amount of the decline is insignificant. A similar trend is apparent in the non-booked singleton group.

Such considerations suggest that the major causes of the reduction in the perinatal mortality rate may be found in a real reduction of the causes of neonatal death and stillbirth among infants of a birth weight of over 4 pounds and upwards rather than in the reduced incidence of the non-booked case group. This suggestion is in keeping with the decline in the neonatal mortality rate and stillbirth rate of the general community.

While this publication deals with the comparison of the perinatal mortality rates for different periods in the same hospital it should not be lost sight of that the method used has a wider application.

Neonatal mortality rates vary from county to county, city to city and country to country. Therefore, unless it can be shown that the incidences of premature birth and plural birth are the same everywhere, the comparison of neonatal mortality rates is always to some extent fallacious. It is doubtful whether there is a central or local authority in possession of accurate knowledge of the incidence of birth weight within its area over a period of even a few years.


## Summary

(1) A method of standardizing the perinatal mortality rate of a maternity hospital is suggested. It takes account of the varying incidence of birth weight, plural pregnancy, and non-booked cases.

(2) The study is based on 5,353 births in the 2-year period 1939–40 and 13,073 births in the 4-year period 1948–51. All the births occurred in the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh.

(3) It is shown that (*a*) the apparent decline in the perinatal mortality rate from 129.1 per 1,000 total births for the years 1939–40 to 72.6 per 1,000 total births for the period 1948–51 is 40 per cent greater than the decline shown by the corresponding standardized perinatal mortality rates of 80.44 for the period 1939–40 and 55.25 for the period 1948–51.

(*b*) The decline in the perinatal mortality rate becomes less with a fall in the birth weight.

(*c*) The major cause of the decline in the perinatal mortality rate is a reduction of the causes of perinatal deaths and not a reduction in the incidence of the non-booked case.


## Reference

Thomson, J. (1952): *J. Obstet. Gynaec. Brit. Emp.*, **59**, 483.

# MULTIPLE PRIMARY CARCINOMATA OF UTERUS

BY

MOSTYN P. EMBREY, B.Sc., M.D., F.R.C.S., M.R.C.O.G.

*First Assistant, Nuffield Department of Obstetrics and Gynaecology*
*University of Oxford*

THE co-existence of multiple primary malignant tumours in one individual is not the rarity it was once thought to be, and since the early part of this century numerous series of cases have been reported, including those of Major (1918), Warren and Gates (1932) and Hurt and Broder (1933). The occurrence of multiple primary malignant tumours in a single organ is much more rare. With the exception of the skin where rodent ulcers are multiple in approximately 5 per cent of cases, it is least infrequent in the intestinal tract, and most surgeons will be familiar with examples of multiple malignancy in large gut or stomach. In the female genital tract the phenomenon is definitely rare and published reports remain few. The following case, therefore, may be deemed worthy of comment.

## CASE REPORT

Mrs. E. T., age 42, para-1, was admitted to the Radcliffe Infirmary in October 1952. She gave a history of a heavy bloodstained discharge for 6 months associated with dragging lower abdominal pain and backache. The menstrual periods were normal. Pelvic examination revealed the cervix patulous with polypoid material within the canal, the uterus anteverted and moderately enlarged, with ill-defined indurated swellings in both lateral fornices. Diagnostic curettage produced friable and obviously malignant material, both from the cervical canal and the uterine body. Preliminary irradiation was carried out.*

Pathological examination of the tumour fragments removed showed a not well differentiated adenocarcinoma, thought to be probably corporeal in origin. Laparotomy 1 week after curettage revealed a bulky uterus with bilateral solid ovarian tumours, each nearly the size of a tennis ball with numerous inflammatory adhesions to the back of the uterus and in the pelvis, and some parametric infiltration especially on the right side. There was no free fluid and no other evidence of extension of the growth. An extended total hysterectomy and bilateral salpingo-oöphorectomy was performed, a cuff of vagina enclosing the cervix. Convalescence was uneventful and treatment was concluded by further radiotherapy.*

*Pathological Report*

The uterus was symmetrically enlarged and measured 9.5 cm. × 6.5 cm. The endocervix contained a fungating tumour measuring 4 cm. × 2.5 cm. In the fundus the endometrium was ragged and polypoid, being involved in a diffuse, papillomatous growth, but between this area and the endocervix there was at least 1 cm. of normal-looking endometrium. Both ovaries were enlarged and nodular, the left measuring 6 × 4 × 4 cm., the right 5.5 × 4 × 3 cm., the cut surface of each showing the presence of scattered cystic and solid areas, the cysts being filled with gelatinous fluid.

Microscopically the squamous epithelium of the pars vaginalis of the cervix was normal. The endocervical gland tubules in the region of the external os were somewhat hyperplastic and the stroma infiltrated with small, round cells. Deeper in the endocervix the lining epithelium was ulcerated, the base of the ulcer being formed superficially by necrotic material infiltrated with inflammatory cells and more deeply by vascular granulation tissue, with masses of irregularly proliferating epithelial cells giving the appearance of an epidermoid carcinoma of the cervix, Broder's Grade III (Fig. 1).

Traced towards the fundus the mucosa presented the structure of an atrophic, non-secretory endometrium (Fig. 2) which eventually gave place to the appearances of a well differentiated papilliferous adenocarcinoma of corpus, Broder's Grade II, made up of irregular endometrial tubules arranged in a papilliferous fashion about a stroma of loose cellular connective tissue (Fig. 3).

Both ovaries presented somewhat similar appearances, with widespread areas showing the histological structure of an adenocarcinoma, in places papilliferous, elsewhere having a poorly developed acinar structure (Fig. 4).

*Radiotherapy consisted of:

(1) Radium: uterus 50 mg., vagina 75 mg., for 30 hours. One week pre-operatively.

(2) Radium: vagina 75 mg. for 22 hours. One week post-operatively. Repeated in one week.

(3) X-ray therapy 3,000 r.

FIG. 1
Epidermoid carcinoma of cervix. ×200

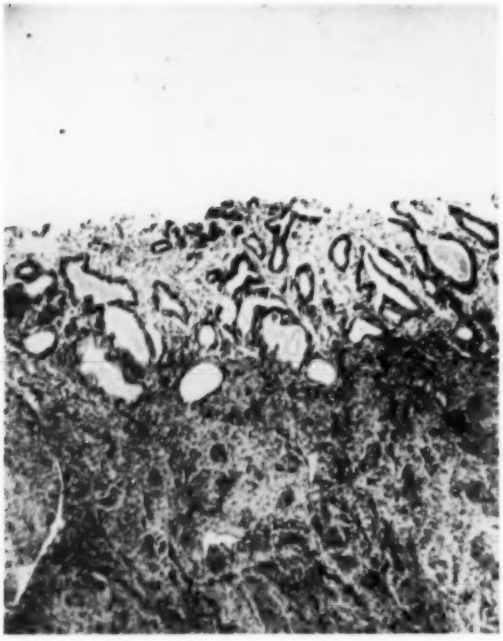


FIG. 2

Benign endometrium separating cervical and corporeal growths. ×200

FIG. 3
Papilliferous adenocarcinoma of corpus. ×200

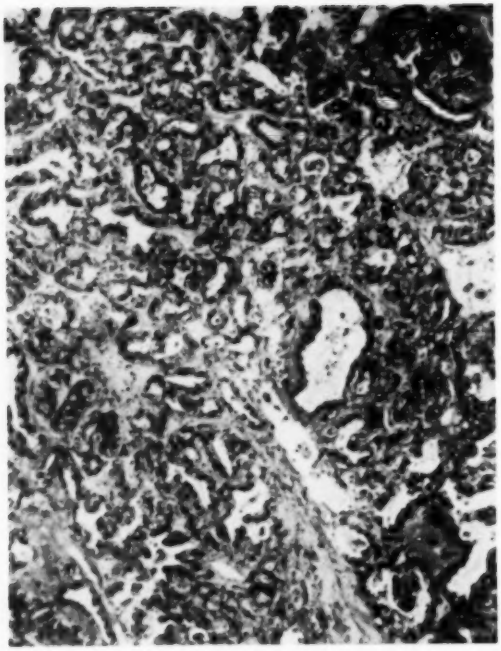


FIG. 4
Adenocarcinoma of left ovary. ×200

## Comment

Before two malignant neoplasms can be assumed to be separate primary tumours, the possibility of one being a direct extension or metastasis of the other must be excluded. It is essential, therefore, that the tumours should arise in different sites, be clearly independent of each other and that they should possess distinct morphological characteristics.

These criteria may be tolerably easy to satisfy when the tumours occur in different organs, but in a single organ the problem is more difficult and one must beware of mimicry. Thus in the uterus two quite distinct histological patterns, one glandular, one squamous, may be seen side by side, but pathological opinion no longer suggests that the adenoma-acanthoma is other than a single tumour in which the cancer cells show an unusual degree of pleomorphism. Again, a carcinoma may invade the musculature to reappear on the mucosa at some distant point. A carcinoma of the corpus may, by implantation or retrograde lymphatic spread, give rise to a cervical neoplasm, while a carcinoma of the cervix not infrequently metastasizes to the body, but none of these represents double primary malignancy. In the case now described the 2 uterine tumours were clearly distinct histologically and anatomically. The endocervical growth was a squamous epithelioma, that in the corpus an adenocarcinoma. The tumours were widely separated and no suggestion of continuity or transition from one to the other could be detected. There seems little doubt that each was a primary neoplasm. No obvious connexion existed between the uterine and ovarian tumours, which possessed some individual characteristics, and the view may be taken that the ovarian tumours, too, represented primary malignancy. But the uterine and ovarian neoplasms were essentially similar in morphology, and it is probable that the minor differences between them were no more than could be accounted for by their different location, and that the ovarian tumours were metastases from the adenocarcinoma of the corpus uteri.

Among comparatively few reports of double primary malignant tumours in the uterus, it would seem that the combination of carcinoma and sarcoma is most common, though its exact frequency is difficult to estimate. Such confusion of nomenclature exists in the literature that it is very difficult to segregate those cases in which carcinoma and sarcoma existed in quite separate tumours from various mixed tumours described under such names as carcinoma-sarcomatoides and carcinoma-sarcoma. Nevertheless, there can be little doubt of a good many recorded examples; Hertel (1912) reported carcinoma of the cervix in cases of uterine sarcoma, while the co-existence of sarcoma and carcinoma of the corpus has been described by Poole (1943) and others.

The simultaneous growth of two carcinomata with distinct morphological characteristics remains uncommon. Goldstine (1935) described a case of squamous carcinoma of the portio and adenocarcinoma of the fundus. Counseller and Butsche (1936) reported 1 case with a mixed epithelioma/adenocarcinoma at the internal os, and an adenocarcinoma at the left cornu; and a second case with adenocarcinoma (Broder's Grade III) of the cervix, and adenocarcinoma (Broder's Grade II) of the fundus. In a case of Smith and Masson's (1939) there was a squamous epithelioma of the cervix and an adenocarcinoma arising in a uterine adenomyoma. Maliphant (1943) described a case in which there was a diffuse adenocarcinoma of the corpus, and a squamous cell carcinoma of the cervix.

Most multiple primary malignant tumours of the uterus have occurred synchronously, but Jacox, Major and Baker (1939) described a case in which a mixed tumour with adenocarcinomatous, epitheliomatous and sarcomatous elements occurred 16 years after successful irradiation of an epithelioma of the cervix, and Berry (1950) published a case in which, 8 years after irradiation of an epithelioma of the cervix, there was a sarcomatous degeneration of a fibroid, and an adenocarcinoma thought to originate in the fundus.

The chief importance of the study of multiple malignancy lies in any bearing it may have on the aetiology of cancer.

In this connexion, statistics indicate that the occurrence of multiple primary malignant

tumours in the same individual is more than a matter of chance. Warren and Gates (1932) maintained that it happens too often for this and have been supported in this view by Bugher (1934) and Burke (1936), while these studies have also shown that the average expectancy of multiple primary malignancy is far exceeded in paired organs and functionally related organs.

It would appear that an individual with one malignant growth provides fertile soil for the development of a second tumour. This implies that the risk of developing cancer is not evenly spread over the population, so that some individuals are more susceptible than others or are exposed to influences bringing about its development. When double primary tumours affect the same organ it may be, as Ewing (1928) suggested, that the second tumour results from local conditions produced by the first.

I wish to express my thanks to Professor J. Chassar Moir for permission to publish this paper.

## References

Berry, C. D. (1950): *Amer. J. Obstet. Gynec.*, **60**, 1385.
Bugher, J. C. (1934): *Amer. J. Cancer.*, **21**, 809.
Burke, M. (1936): *Amer. J. Cancer*, **27**, 316.
Counseller, V. S., and Butsche, W. L. (1936): *Amer. J. Obstet. Gynec.*, **31**, 628.
Ewing, J. (1928): *Neoplastic diseases.* Saunders, Philadelphia. p. 37.
Frank, R. T. (1931): *Gynaecological and obstetrical pathology.* Appleton, New York.
Goldstine, M. T. (1935): *Amer. J. Obstet. Gynec.*, **20**, 137.
Hertel, W. (1912): *Mschr. Geburtsh. Gynäk.*, **36**, 325. (Quoted by Frank, R. T., 1931, p. 244.)
Hurt, H. H., and Broder, A. C. (1933): *J. Lab. clin. Med.*, **18**, 765.
Jacox, H. W., Major, G., and Baker, M. R. (1939): *Radiology*, **32**, 51.
Major, R. H. (1918): *Johns Hopk. Hosp. Bull.*, **29**, 223.
Maliphant, R. G. (1943): *J. Obstet. Gynaec. Brit. Emp.*, **50**, 59.
Poole, C. S. (1943): *Amer. J. Obstet. Gynec.*, **46**, 434.
Smith, C. H., and Masson, J. C. (1939): *Proc. Mayo Clin.*, **14**, 476.
Warren, S., and Gates, O. (1932): *Amer. J. Cancer*, **16**, 1358.

# THE AETIOLOGY OF ANENCEPHALY

BY

H. VINCENT CORBETT, M.Sc., M.D., F.R.C.S., M.R.C.O.G., M.M.S.A.
*Consultant Obstetrician and Gynaecologist, St. Helens Hospitals, Lancs.*
*Visiting Consultant Gynaecologist, Noble's (I.O.M.) Hospital, Douglas, Isle of Man*

## INTRODUCTION

THE obvious approach to the problem of foetal malformations is the initial determination of their incidence in various groups of patients. Perhaps the most defined malformation and the one least likely to be overlooked is anencephaly. The present paper is devoted to a study of the incidence of this abnormality alone without associated deformities.

Similar enquiries have been carried out by Malpas (1937), whose material was derived entirely from the Liverpool Maternity Hospital, and by Record and McKeown (1949) who drew their material from the total births in Birmingham over a given period. This material was drawn from several sources whose population was known and in which the complete records of anencephalic births were available.

## RESULTS

*Isle of Man.* This is mainly a rural area with a virtually closed population which is largely homogeneous. Most of the births took place in hospital and the records are complete from about 1935 to 1950. The general incidence of anencephaly was 0.11 per 1,000 births.

*Wrexham.* This is a mixed industrial and agricultural area with a heterogeneous population. The incidence was 0.11 per 1,000 births.

*Billinge.* This is a self-contained coal-mining area and the incidence was 0.22 per 1,000 births.

*St. Helens.* This is a mixed industrial area with an incidence of 0.23 per 1,000 births.

*Liverpool Maternity Hospital.* This is a large teaching hospital into which many cases of anencephaly find their way from outside areas. The incidence was 0.56 per 1,000 births.

*Caernarvon.* This is a closed rural, largely Welsh-speaking area with an incidence of 0.20 per 1,000 births.

*Whiston.* This is a unit admitting cases from a mixed population mainly industrial, the incidence being 0.23 per 1,000 births.

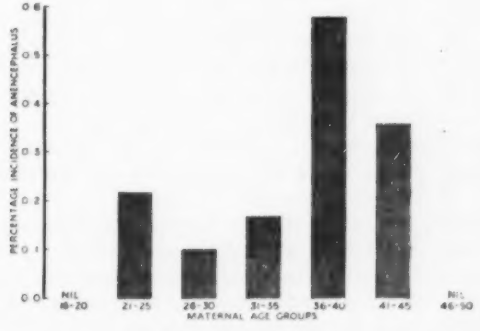



FIG. 1. Billinge.

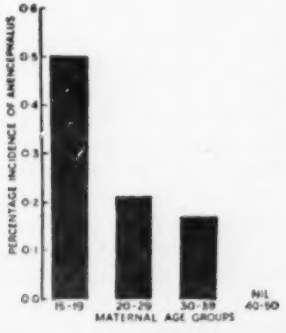



FIG. 2. Caernarvon.

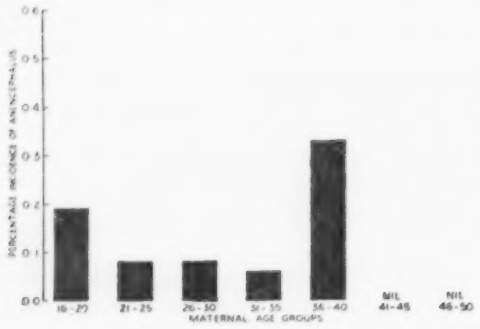



FIG. 3. Isle of Man.

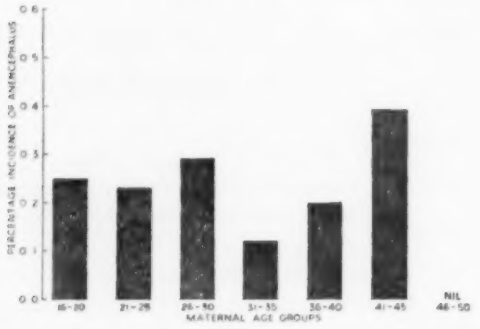



FIG. 4. St. Helens.

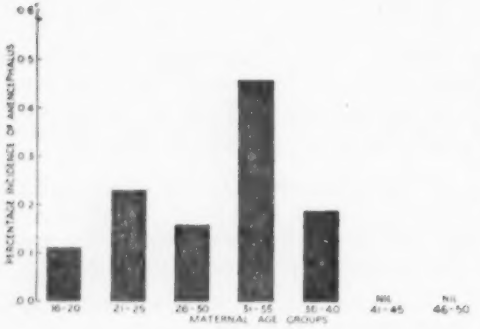



FIG. 5. Whiston.

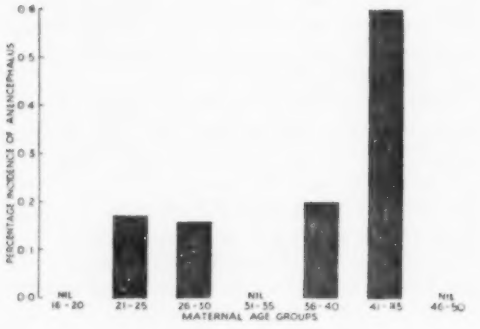



FIG. 6. Wrexham (Hospital).

## DISCUSSION

In a similar investigation based on data from the Liverpool Maternity Hospital, Malpas (1937) gives a figure of 0.31 per 1,000 births. A further review of cases occurring in this hospital since 1937 and undertaken in the course of this enquiry revealed a still higher incidence of 0.56 per 1,000 births. This shows that the results based on the practice of a teaching hospital are not a true index of the incidence of the condition. In this regard the lower incidence of anencephaly when only booked cases were analysed is illustrated by the figure of 0.14 per 1,000 births obtained by Carter (1950). It will be seen that the figures in these differing types of population apart from the Liverpool Maternity Hospital correspond closely with those recorded from Birmingham.

### *Relation of Incidence of Anencephaly to Locality, Parity and Maternal Age*

The results obtained from the different areas of Lancashire, North Wales and the Isle of Man (with the exception of the Caernarvon figures, which were unsuitable for analysis, and those from a domiciliary practice in the Wrexham area in which no cases of anencephaly occurred) have been subjected to statistical analysis, and the observations of Professor R. G. Harrison, of the Department of Anatomy of the University of Liverpool are set out below.

" In all cases the Chi$^2$ test has been used and the following results were obtained.

" When the incidence of anencephalic births at the Liverpool Maternity Hospital is compared with that in the Isle of Man $\chi^2 = 28.57$ $n = 1$ $P = 0.001$ which is highly significant. This

[*Continued on page* 911

TABLE I

*Author's Series*

*Total Number of Cases* — 260. *Total Births* — 92,575.

*Percentage Incidence in Total Population* — 0.28.

| Locality | Age Groups | | | | | | | Total No. (All Groups) | Total Births | Percentage Incidence |
|---|---|---|---|---|---|---|---|---|---|---|
| | 16–20 | 21–25 | 26–30 | 31–35 | 36–40 | 41–45 | 46–50 | | | |
| Liverpool Maternity Hospital ... ... | Not analyzed for Age Groups | | | | | | | 124 | 21,997 | 0.56 |
| Billinge Hospital ... ... ... | 0 | 9 | 3 | 3 | 6 | 1 | 0 | 22 | 10,076 | 0.22 |
| St. Helens Hospitals ... ... ... | 2 | 8 | 9 | 2 | 2 | 1 | 0 | 24 | 10,100 | 0.23 |
| Caernarvon and Anglesey Infirmary ... | 3 | 8 | 7 | 5 | 2 | 0 | 0 | 25 | 12,265 | 0.20 |
| Trevalyn Manor Maternity Hospital, Wrexham ... ... ... ... | 0 | 2 | 2 | 0 | 1 | 1 | 0 | 6 | 4,161 | 0.11 |
| Widnes (Domiciliary) ... ... ... | 2 | 12 | 8 | 4 | 2 | 0 | 0 | 28 | 15,231 | 0.18 |
| Wrexham (Domiciliary) ... ... | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1,352 | – |
| Noble's (I.O.M.) Hospital ... ... | 1 | 2 | 2 | 1 | 3 | 0 | 0 | 9 | 8,065 | 0.11 |
| Whiston County Hospital ... ... | 1 | 7 | 4 | 8 | 2 | 0 | 0 | 22 | 9,328 | 0.23 |
| *Other British Series* | | | | | | | | | | |
| (1937) Malpas (Liverpool Maternity Hospital) ... ... ... ... ... ... ... ... | | | | | | | | 43 | 13,964 | 0.31 |
| (1950) Carter (Queen Charlotte's Hospital) (Booked Cases only) ... ... ... ... ... | | | | | | | | 21 | 14,813 | 0.14 |

TABLE II

*Maternal Age Incidence of Anencephalus*
(*See also* Figs. 1–6)

| Age groups | | Normal births | Percentage of normal births | Number of anencephalies | Percentage incidence |
|---|---|---|---|---|---|
| *Billinge* (Fig. 1) | | | | | |
| | 16–20 | 816 | 7.9 | 0 | — |
| | 21–25 | 3,074 | 29.9 | 9 | 0.22 |
| | 26–30 | 3,126 | 30.0 | 3 | 0.10 |
| | 31–35 | 1,742 | 17.0 | 3 | 0.17 |
| | 36–40 | 1,028 | 10.0 | 6 | 0.58 |
| | 41–45 | 270 | 2.6 | 1 | 0.36 |
| | 46–50 | 20 | 0.19 | 0 | — |
| *Caernarvon* (Fig. 2) | | | | | |
| | 15–19 | 389 | 5.0 | 2 | 0.50 |
| | 20–29 | 4,252 | 54.0 | 9 | 0.21 |
| | 30–39 | 2,853 | 36.0 | 5 | 0.17 |
| | 40–50 | 330 | 5.0 | 0 | — |
| *Isle of Man* (Fig. 3) | | | | | |
| | 16–20 | 514 | 6.3 | 1 | 0.19 |
| | 21–25 | 2,362 | 29.0 | 2 | 0.08 |
| | 26–30 | 2,425 | 30.0 | 2 | 0.08 |
| | 31–35 | 1,633 | 20.0 | 1 | 0.06 |
| | 36–40 | 909 | 11.0 | 3 | 0.33 |
| | 41–45 | 214 | 2.6 | 0 | — |
| | 46–50 | 8 | 0.1 | 0 | — |
| *St. Helens* (Fig. 4) | | | | | |
| | 16–20 | 774 | 7.3 | 2 | 0.25 |
| | 21–25 | 3,391 | 32.0 | 8 | 0.23 |
| | 26–30 | 3,018 | 30.0 | 9 | 0.29 |
| | 31–35 | 1,646 | 15.5 | 2 | 0.12 |
| | 36–40 | 1,000 | 9.4 | 2 | 0.20 |
| | 41–45 | 256 | 2.3 | 1 | 0.39 |
| | 46–50 | 15 | 0.14 | 0 | — |
| *Whiston* (Fig. 5) | | | | | |
| | 16–20 | 851 | 9.5 | 1 | 0.11 |
| | 21–25 | 2,986 | 32.4 | 7 | 0.23 |
| | 26–30 | 2,471 | 29.0 | 4 | 0.16 |
| | 31–35 | 1,716 | 19.0 | 8 | 0.46 |
| | 36–40 | 1,011 | 11.3 | 2 | 0.19 |
| | 41–45 | 268 | 3.0 | 0 | — |
| | 46–50 | 25 | 0.3 | 0 | — |
| *Wrexham* (*Hospital*) (Fig. 6) | | | | | |
| | 16–20 | 305 | 7.0 | 0 | — |
| | 21–25 | 1,172 | 27.7 | 2 | 0.17 |
| | 26–30 | 1,217 | 28.8 | 2 | 0.16 |
| | 31–35 | 813 | 19.0 | 0 | — |
| | 36–40 | 460 | 10.9 | 1 | 0.20 |
| | 41–45 | 157 | 3.7 | 1 | 0.60 |
| | 46–50 | 7 | 0.2 | 0 | — |
| *Wrexham* (*Domiciliary*) | | | | | |
| | 16–20 | | | | |
| | 21–25 | | | | |
| | 26–30 | 1,352 | | nil | nil |
| | 31–35 | | | | |
| | 36–40 | | | | |

TABLE III

*Incidence of anencephaly in relation to parity*

| Locality | Percentage incidence of anencephaly in | | Percentage (in total populations) of | |
|---|---|---|---|---|
| | Primigravidae | Multigravidae | Primigravidae | Multigravidae |
| Billinge ... ... ... ... ... | 54 | 46 | 54 | 46 |
| Caernarvon and Anglesey ... ... | 46 | 56 | 49 | 51 |
| Isle of Man ... ... ... ... | 60 | 40 | 47 | 53 |
| St. Helens ... ... ... ... | 50 | 50 | 48 | 52 |
| Whiston ... ... ... ... ... | 45 | 55 | 45 | 55 |
| Wrexham ... ... ... ... | 66 | 34 | 49 | 51 |
| Average ... ... ... ... | 53 | 47 | 49 | 51 |

means either that a bigger proportion of anencephalics were delivered in hospital in Liverpool than in the Isle of Man or that the indigenous population of the Isle of Man is less likely to produce anencephalics. The former alternative seems the more likely. There is no significant difference between the incidence of anencephaly in the other localities, and when Malpas' (1937) figures are compared with your figures for the Liverpool Maternity Hospital, they mean that either the number of anencephalics has increased or that more such cases have been admitted to hospital; I think you will agree that it is probably the latter. I have noted your observations on the relationship of anencephaly to parity, and to maternal age groups. While I agree with your conclusions on the lack of relation of anencephaly to parity (I do not think it is even necessary to perform a statistical analysis here) I think it is imperative it should be undertaken on the relation of incidence of anencephaly to maternal age groups before any definite conclusion is made. Thus when the percentage incidence of anencephaly was compared with mean age groups as shown in Table IV (excluding the data for Caernarvon and the Wrexham domiciliary group), by the estimation of the correlation coefficient, the coefficient is found to be 0.699, which is not significant, and is less than twice the standard error (0.447). There is, therefore, no significant correlation between maternal age and percentage incidence of anencephaly. If the Wrexham domiciliary group of cases and those from Caernarvon had been included, the result would have been even more insignificant."

TABLE IV

| Mean age | Percentage incidence of anencephaly |
|---|---|
| 18 | 0.123 |
| 23 | 0.216 |
| 28 | 0.162 |
| 33 | 0.185 |
| 38 | 0.318 |
| 43 | 0.258 |

These views conflict with those of Malpas (1937) and with those of Record and McKeown (1949).

## CONCLUSIONS

Anencephaly appears to have a very constant incidence, which seems to be unaffected by locality, parity and maternal age. The absence of positive differences shows that at the moment and so far as present knowledge goes no environmental factor can be held responsible for its incidence and this being so the question of whether anencephaly is due to hereditary or genetic factors alone is still *sub judice*.

I am greatly indebted to Mr. Percy Malpas under whose guidance this investigation was

initiated some years ago, and whose help and encouragement have been constant every since. I would also gratefully acknowledge the assistance afforded me by Mr. Arthur A. Gemmell who allowed me access to the records of the Liverpool Maternity Hospital. I was also given the utmost help by my friends in charge of the other departments mentioned, and by their Sisters in sub-charge. My thanks are also due to Professor Harrison for his most willing help with the statistical analysis.

## References

Carter, C. O. (1950): *J. Obstet. Gynaec. Brit Emp.*, **57**, 897 (and Personal Communication).

Malpas, P. (1937): *J. Obstet. Gynaec. Brit. Emp.*, **44**, 434.

Record, R. G., and McKeown, T. (1949): *Brit. J. soc. Med.*, **3**, 183.

# SPONDYLOLISTHESIS AND PREGNANCY

## A Case Report

BY

CHARLES J. CHAMP, M.D., M.R.C.O.G.

*Senior Registrar, Department of Obstetrics and Gynaecology, Royal Free Hospital, London*

SPONDYLOLISTHESIS is an uncommon but important cause of pelvic deformity. Few cases have been reported in relation to obstetrics in recent years. Johnstone (1934) described a severe case in pregnancy which ended in a spontaneous delivery; Soiva (1948) reported a case delivered by Caesarean section and could find only 10 other reported cases since 1927.

### CASE REPORT

Mrs. M. T., aged 43, booked at the Royal Free Hospital for her 3rd confinement when she was 8 weeks pregnant. The expected date of delivery was in early December 1952.

She had had 2 previous full-time spontaneous deliveries in 1929 and 1933, the infants weighing respectively 7½ pounds (3.4 kg.) and 10 pounds (4.5 kg.). Each labour was of short duration.

Shortly after the second delivery, the patient experienced severe low backache, associated with genital prolapse. Anterior and posterior colpoperineorrhaphy was performed in 1935, when the patient was only 25 years old.

There was no history of other serious illnesses or operations. The patient remarried in 1949 and the present pregnancy was the first by her second husband.

Pregnancy continued uneventfully until the 32nd week, when the patient complained of severe low backache, which radiated down her left leg. X-ray of the lumbar spine showed spondylolisthesis of the body of the lumbar vertebra on the upper surface of the sacrum, a second-degree deformity according to the classification of Meyerding (1934).

On further inquiry into her past history the patient could recollect no severe trauma to her back, but said she often experienced severe backache after hard work.

More detailed examination showed the classical signs of spondylolisthesis (Figs. 1 and 2). The abdomen was pendulous and the lower ribs closely approximated to the iliac crests. On inspection of the back the spine of L.5 was prominent and above this a well-marked furrow extended upwards in the midline to the level of L.1, corresponding to the forward displacement of the vertebral column at the body of L.5. The rhomboid of Michaelis was flattened from above downwards.

At subsequent antenatal examinations the foetus presented by the vertex but the head remained very high above the pelvic brim. On vaginal examination at the 38th week the sacral promontory and lower border of L.5 were reached at 4¾ inches (11.9 cm.). The foetal head could not be made to engage in the brim.

X-ray pelvimetry (Figs. 3 and 4) showed the body of L.5 overlapping the pelvic brim, giving the effect of a bow-like outline as described by Johnstone. The pseudo-conjugate taken from the upper posterior border of the symphysis pubis to the nearest part of L.5 measured 4.2 inches (10.5 cm.). The fore-pelvis was narrowed and the subpubic angle measured 75 degrees.

Elective lower segment Caesarean section was performed on 29th November, 1952, for three relative indications: (i) cephalo-pelvic disproportion, (ii) the previous repair operation, and (iii) as the patient was 42 years old and this was her first child by her second husband.

The puerperium was uneventful and the backache was much improved when the patient left hospital. At postnatal examination on 8th January, 1953, the patient was very well and her backache had improved considerably. She was referred to the orthopaedic department for further treatment.

### COMMENT

Spondylolisthesis is a progressive condition almost certainly made worse by pregnancy, particularly in a multigravida with lax abdominal musculature, where a great strain is placed upon the lumbosacral angle from the pendulous abdomen and increased lumbar lordosis. In addition, the supporting ligaments of this joint are softened in pregnancy due to hormonal action.

Thus a history of previous uneventful vaginal deliveries must not lead to the assumption that subsequent confinements will be normal.

Severe spondylolisthesis causes the pelvis to become funnel-shaped owing to alteration in the posture of the patient, and arrest in labour may occur in the mid-cavity or outlet of the pelvis.

In the case reported the patient had previously delivered a baby weighing 10 pounds, but it is doubtful whether the present child, weighing only 8½ pounds, would have passed through the pelvis without difficulty.

I wish to thank Miss Gladys Hill, Director of the Department of Obstetrics and Gynaecology at the Royal Free Hospital, for permission to publish this case, and Mr. Sheppard for the photographs.

## References

Johnstone, R. W. (1934): *Trans. Edinb. obstet. Soc.*, **55**, 29.

Meyerding, H. W. (1934): *Proc. Mayo Clin.*, **9**, 666.

Soiva, K. (1948): *Acta obstet. gynec. scand.*, **28**, 137.

FIG. 1
Lateral view of patient with spondylolisthesis showing pendulous abdomen.

FIG. 2
Oblique view of patient with spondylolisthesis showing furrow over lumbar spine and flattened rhomboid of Michaelis.

C.J.C.

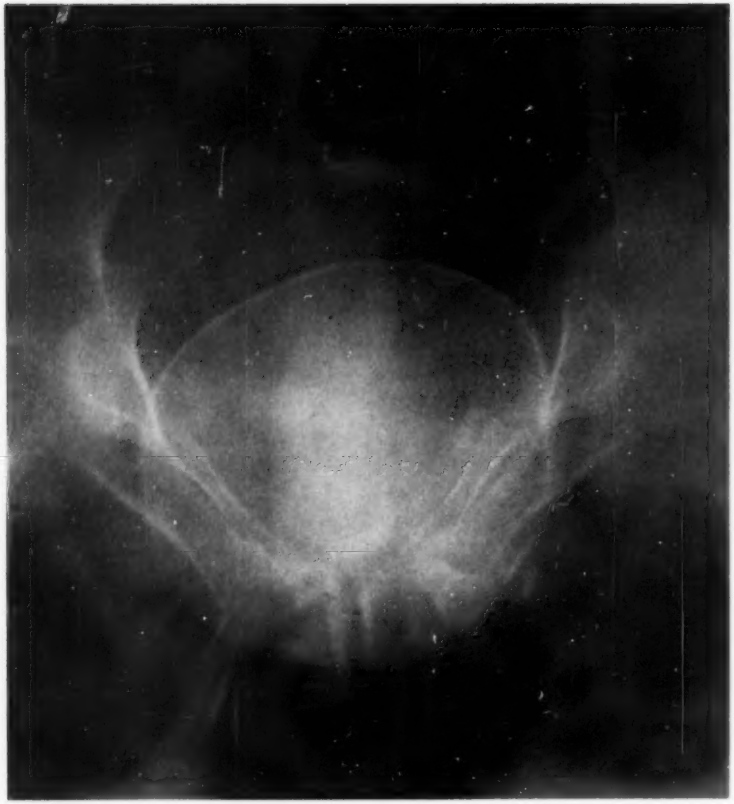


FIG. 3

Spondylolisthesis. X-ray pelvimetry of pelvic brim.

FIG. 4
Spondylolisthesis. X-ray pelvimetry. Lateral view.

# KRUKENBERG TUMOUR OF THE OVARIES COMPLICATING PREGNANCY

BY

S. BURKE, M.D., F.R.C.S., D.Obst.R.C.O.G.

*From the Department of Obstetrics and Gynaecology, Post-Graduate Medical School of London*

KRUKENBERG tumours are often reported in the literature, but their association with pregnancy is rare. The case described below is considered to be worth reporting because it presents several unusual features.

## CASE HISTORY

The patient, a primigravida, aged 22 years, was admitted to hospital on 4th May, 1941. According to the menstrual history she was 32 weeks pregnant and had been vomiting for the past fortnight. She complained of severe epigastric pains, frontal headache and insomnia for the same period, and swelling of the legs for the past 3 days. Vomiting, she stated, was becoming increasingly frequent. During the past 2 years she had had occasional attacks of epigastric pain and vomiting for which she had not sought medical attention. The menstrual history had always been normal.

On examination she was found to be somewhat dehydrated, the systolic blood-pressure was 134, and the diastolic 90 mm.Hg., and the urine contained an appreciable amount of albumen. The abdomen was difficult to palpate owing to the generalized tenderness, but the uterus appeared to be much larger than a 32-weeks pregnancy. The foetal heart could be heard, and the vertex was presenting. Pelvic measurements were normal; there was considerable oedema of the ankles. A provisional diagnosis of pre-eclamptic toxaemia was made and treatment commenced for that condition. Vomiting, however, continued frequently, and because of continued deterioration in the patient's condition induction was performed by rupture of the membranes. At the same time an intravenous infusion of 5 per cent glucose was begun. Vomiting continued with alarming frequency during the day, and labour began in the early morning of 6th May. At this time the foetal heart could still be heard. After labour had been in progress about 3 hours the patient became very collapsed. Further examination of the abdomen now showed the presence of a large quantity of free fluid, mainly in the right flank. There could also be felt a large round tumour about the size of a foetal head in the right hypochondrium. This tumour was mobile, could be palpated quite readily, and appeared to be a separate entity from the contracting uterus. The foetal heart could no longer be heard. Abdominal paracentesis was performed, and blood-stained fluid obtained. A diagnosis of torsion of an ovarian cyst and possibly of malignancy was considered, but the patient's condition was such as to preclude laparotomy.

An hour later a normal delivery occurred of a fresh, stillborn, male foetus weighing 3 pounds 8 ounces, showing no external congenital abnormalities.

The patient's colour and pulse improved rapidly after delivery and vomiting ceased for a time. The intravenous infusion, however, was continued. It was now possible to feel the tumour more easily; it was freely mobile. Vomiting began again later in the day, and the patient's condition gradually deteriorated further, death occurring on 8th May.

### *Postmortem Report*

Several pints of blood-stained fluid were evacuated. Both ovaries were enormously enlarged, roughly spherical in shape and quite free of adhesions. The right ovary was twisted three times on its pedicle and was deep red in colour. The left ovary, somewhat smaller, was prolapsed into the pouch of Douglas. The right ovary weighed 6 pounds, and the left 3 pounds 6 ounces. There was a firm nodular mass extending along almost the whole length of the greater curvature of the stomach, and complete pyloric stenosis was present. The gastro-colic glands were enlarged and neoplastic. A chain of enlarged firm and rubbery glands, obviously neoplastic, extended well down the aorta. No secondary growths were present in the liver, and there was no evidence of peritoneal dissemination.

### *Histology*

The stomach was extensively invaded by colloid carcinoma and both the ovaries were destroyed by similar growth (Fig. 1). In the right ovary torsion appeared to have occurred, and the tissue was suffused with recent haemorrhage. The appearances were those of a colloid carcinoma with advanced mucinous degeneration. "Signet ring" cells were present (Fig. 2). The growth in this case had a meshwork of rather degenerate connective tissue strands with a large amount of mucinous debris in the interstices, and epithelial cells in various stages of degeneration.

## Discussion

Krukenberg (1896), though his concept of the pathogenesis of this type of ovarian tumour was mistaken, laid down certain criteria. He stated that the tumours grew to a large size, were almost invariably bilateral, the external surface was smooth or moderately lobulated and the general shape of the ovary was maintained. The tumours were not fixed or adherent, and were almost invariably accompanied by ascites. As regards the microscopical appearances, he laid great stress on the somewhat dense fibrocellular stroma and the presence of " signet ring " cells.

Jarcho (1938) pointed out the greater variation in these tumours, however, and showed that " signet ring " cells were not always present.

Leffel, Masson and Dockerty (1942) were of the opinion that in some cases the stroma might be oedematous or almost entirely blotted out by mucinous changes. It is generally agreed that mucoid change is an essential feature of this tumour. However, Novak (1947) and Willis (1948) firmly believe that all Krukenberg's original criteria should be fulfilled. It is felt that the tumour described above meets Krukenberg's requirements.

From the few references in the literature to Krukenberg tumours complicating pregnancy, only 2 have been found where the pregnancy continued over 28 weeks. Burdsinsky (1908) described a case in a patient aged 26 where a live child was delivered at term by Caesarean section, the patient dying 3 days later. Esau (1933) removed bilateral ovarian tumours from a patient aged 26 shortly after delivery of a live child. No primary tumour was found. This case is of interest because the patient did not die until 2½ years later of gastric carcinoma. Cases of Krukenberg tumour with fairly well advanced pregnancy were also reported by Schmid (1924), Guiroy and Jakob (1928), and Bud (1935), among others.

A review of the literature shows that in all cases the stomach was the primary site. The clinical features were very similar in several cases, albuminuria and excessive vomiting being present. Burdsinsky's case had persistent vomiting and a left ovarian tumour described as the size of a man's head. Schmid's case had a left ovarian tumour described as twice the size of a child's head, which was found prolapsed into the pouch of Douglas and twisted through 180°. Hagstrom (1938) reported a case which as regards symptoms closely paralleled the one described here. The patient was 5½ months pregnant and suffered from continuous vomiting. Here also a diagnosis of pre-eclamptic toxaemia was made, and labour was induced with a Voorhees' bag, the patient dying undelivered 6 hours later.

It would appear from the literature that there has been considerable difficulty in the diagnosis of these cases. The onset of persistent vomiting in the middle or third trimesters of pregnancy, especially when associated with albuminuria and oedema, may lead to an erroneous diagnosis of pre-eclamptic toxaemia. The difficulties are increased when the abdominal enlargement due to the ovarian tumours and ascites suggests the possibility of twins and hydramnios. The possibility that the vomiting may be due to a serious gastric lesion should be borne in mind.

The case reported here presents some unusual features, such as the extreme youth of the patient, and the extent to which the pregnancy progressed in spite of the magnitude of the gastric and ovarian lesions. The acute torsion of the right ovarian tumour which occurred during labour also adds interest to the case.

I am grateful to Professor J. C. McClure Browne for his helpful advice and encouragement in the preparation of this paper, and to Mr. E. V. Willmott for the photomicrographs.

## References

Bud, G. (1935): *Orv. Hetil*, **79**, 146.
Burdsinsky, T. A. (1908): *Zbl. Gynäk.*, **32**, 410.
Esau, P. (1933): *Zbl. Gynäk.*, **57**, 1167.
Guiroy, A. J., and Jakob, A. (1928): *Bull. Soc. Obstét. Gynéc. Paris*, **17**, 535.
Hagstrom, H. T. (1938): *Amer. J. Obstet. Gynec.*, **36**, 498.
Jarcho, J. (1938): *Amer. J. Surg.*, **41**, 538.
Krukenberg, F. (1896): *Arch. Gynäk.*, **50**, 287.
Leffel, J. M., Masson, J. C., and Dockerty, M. B. (1942): *Ann. Surg.*, **115**, 102.
Novak, E. (1947): *Gynecological and obstetrical pathology*. Saunders, Philadelphia. p. 362.
Schmid, H. H. (1924): *Arch. Gynäk.*, **121**, 168.
Willis, R. A. (1948): *Pathology of tumours*. Butterworth, London. p. 408.

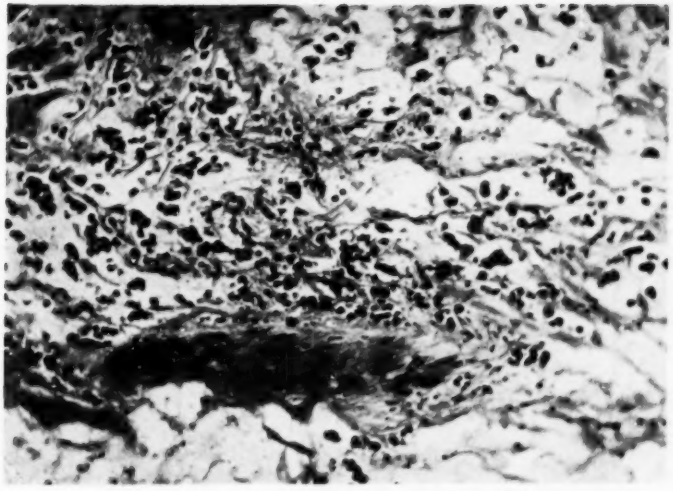


FIG. 1

Stomach showing malignant cells and mucinous degeneration. ×126

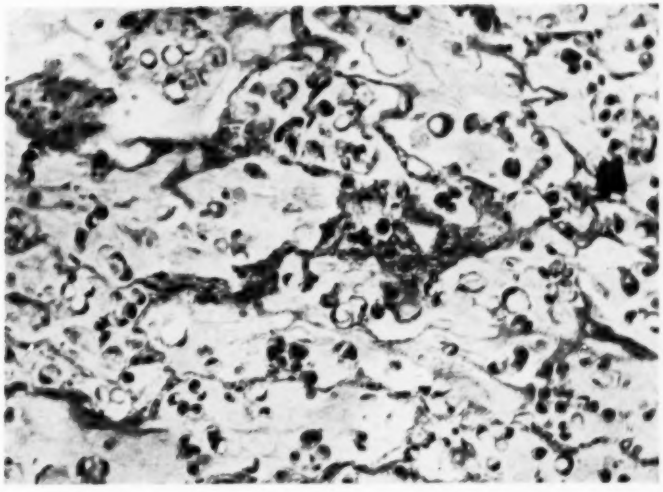


FIG. 2

Ovary showing "signet ring" cells, degenerate connective tissue strands and mucinous debris. ×176

S.B.

# A CASE OF GRANULAR CELL MYOBLASTOMA OF THE VULVA

BY

H. B. WATSON, M.B., F.R.F.P.S., M.R.C.O.G.
*Obstetrician and Gynaecologist, Solihull Hospital*

AND

C. W. TAYLOR, M.B., Ch.B.
*Director of Pathology, The Birmingham and Midland Hospital for Women*

THE rarity of this condition and the associated difficulty in differential diagnosis, clinically and histologically are the reasons for recording this case.

G. H., married, aged 32 years, was admitted on 10th September, 1951. She complained of a small swelling in the right side of the vulva, which had been present for nearly 2 years. It was associated with local itching and had been slowly increasing in size. She stated that the nodule appeared to be softer and less obvious at the time of her periods. Menstruation occurred regularly every 28 days, lasting 4 to 5 days, and there was no vaginal discharge.

She had a spontaneous delivery of a full-time baby 9½ years previously and for approximately 1 year afterwards wore a ring pessary to control a slight prolapse. In 1944 she had received treatment for salpingitis.

On examination, the patient was normally developed. Inspection of the vulva revealed a smooth firm nodule approximately 2 cm. in diameter, situated in the middle third of the lateral aspect of the right labium majus. It was lying in the subcutaneous tissue and could not be separated from the overlying skin. A provisional diagnosis of sebaceous cyst was made. Vaginal examination revealed a slight cystocele, a retroverted uterus of normal size, and a palpably thickened and tender right appendage.

On 11th September, 1951, under Pentothal anaesthesia, the nodule was excised close to its edges and the wound was closed with three silk-worm gut sutures. The patient's postoperative progress was satisfactory and the wound healed by first intention.

The patient was followed up at approximately monthly intervals, and she remained well apart from a flare-up of her pelvic infection in November 1951, which readily responded to shortwave therapy. She was last examined on 6th September, 1952, and was fit and well. There had been no vulval irritation and the scar in the right labium majus was almost imperceptible.

*Operative Specimen*

Naked eye examination showed a solid nodule 1.5 cm. in diameter of firm consistency. The cut surface was yellowish and smooth. A thin layer of intact skin was present.

The possibility of hidradenoma was now considered rather than a sebaceous cyst, and the specimen was submitted for histological examination.

*Histological Report* (W. H. B. 51/2219)

Microscopical examination shows a solid subcutaneous nodule composed of large cells with marked acidophil granular cytoplasm. These cells are of uniform type, resemble myoblasts and extend from beneath the dermis to portions of smooth muscle at the base of the tumour (Figs. 1, 2). Special stains fail to demonstrate striations in any of the granular cells or adjacent muscle fibres. The covering squamous epithelium is intact but in one area shows marked atypical proliferation with projection into the underlying tissues (Fig. 3).

This nodule is a typical granular-cell myoblastoma of uniform type. The tumour cells extend to the line of excision where they intermingle with smooth muscle fibres (Fig. 4) so that the possibility of recurrence must be considered.

## DISCUSSION

Myoblastoma is the name given to a tumour which occurs in striated muscle, usually the tongue; also beneath the skin and mucous membranes. The tumour cells resemble myoblasts, are large and elongated and show markedly granular acidophil cytoplasm. Actual origin from myoblasts is open to doubt and, though striations and mergence into muscle fibres have been demonstrated in lesions of the tongue and skeletal muscle, these features are not seen in the cutaneous nodules. Some authorities, including Willis (1948), consider that the tumour is not necessarily neoplastic and that it may result from trauma. The name myoblastoma may therefore be a misnomer but there is no doubt of the entity of the lesion, and the term granular cell myoblastoma has become accepted as a useful descriptive title.

Confusion has further occurred due to the inclusion under the term myoblastoma of certain malignant anaplastic neoplasms, some of the rhabdomyomatous type. Murphy *et al.* (1949) have differentiated the myoblastomas into two main groups—the uniform and the pleomorphic. The latter type is extremely rare but a few cases showing recurrence and metastases have been recorded. Commonly the tumour is of uniform type, as here described, and is a small, poorly encapsulated, slowly growing benign nodule.

The lesion was first described by Abrikossoff in 1926. In 1951, Sadler and Dockerty were able to review nearly 300 cases from the literature and, of these, 5 were situated in the vulva. The origin in this site is probably simply that of the skin elsewhere with no peculiar local significance. Sadler and Dockerty have suggested that the tumour arises from pluripotent mesenchymal cells.

The associated abnormal proliferation of the covering squamous epithelium, a feature common when the tumour occurs in the tongue or skin, is extremely important. At first sight this change is suggestive of early squamous-cell carcinoma and could be mistaken for this. A wrong interpretation from a biopsy might therefore lead to an unnecessary radical operation. The nature of this pseudomalignant proliferation is unknown, but appears to be reactive when the tumour cells come into contact with the covering epithelium.

A differential diagnosis will always be difficult. The gross appearances usually suggest an innocent lesion, and it is very unlikely that differentiation can be made clinically from sebaceous cyst, hidradenoma, fibroma and similar tumours.

As far as the vulva is concerned, adequate excision and histological study is of paramount importance for every tumour encountered.


## Summary

A case of granular cell myoblastoma of the vulva is recorded.

The nature of the tumour is briefly considered.

Attention is drawn to the pseudomalignant changes in the overlying epithelium.


## References


Abrikossoff, A. (1926): *Virchows Arch.*, **260**, 215.

Murphy, G. H., Dockerty, M. B., and Broders, A. C. (1949): *Amer. J. Path.*, **25**, 1157.

Sadler, W. P., and Dockerty, M. B. (1951): *Amer. J. Obstet. Gynec.*, **61**, 1047.

Willis, R. A. (1948): *Pathology of tumours.* Butterworth, London.

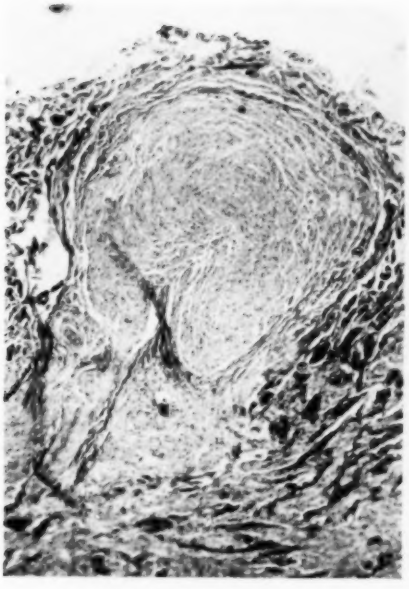


FIG. 1

Portion of subcutaneous nodule consisting of masses of pink-staining granular cells. (H. and E.) ×60

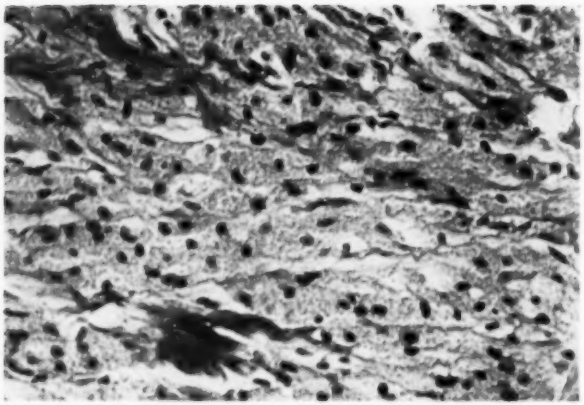


FIG. 2
Higher-power picture showing uniform, plump, elongated cells with granular cytoplasm resembling myoblasts. ×270

FIG. 3

Atypical proliferation of covering squamous epithelium of pseudo-malignant type. The granular cells are in direct contact with the epithelium. ×60

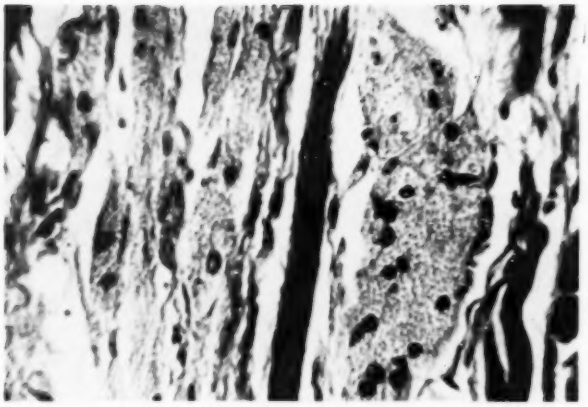


FIG. 4

The granular cells intermingled with smooth muscle fibres at the base of the tumour. No striations could be demonstrated. ×420

# AN UNUSUAL CASE OF SECONDARY POSTPARTUM HAEMORRHAGE NECESSITATING HYSTERECTOMY

BY

J. K. RUSSELL, M.B., M.R.C.O.G.

*Lecturer in Obstetrics and Gynaecology, University of Durham*

THE necessity for hysterectomy in a case of postpartum haemorrhage is so unusual that the following case is considered of sufficient interest to record.

The patient, a gravida-6, aged 39 years, had a bad past obstetric history. Her first baby, weight 6 pounds, was stillborn following a forceps delivery. The second and third babies, weighing 7 pounds and 6 pounds at birth, are alive and well. The fourth baby, weight 8 pounds, was stillborn following forceps delivery. The fifth pregnancy resulted in twins, both weighing 5 pounds. One of these was stillborn. Primary postpartum haemorrhage occurred after the fourth and fifth deliveries and blood transfusions were given. She was known to have a slight degree of pelvic contraction (true conjugate 10 cm.).

In her present pregnancy the patient was referred to the antenatal clinic at the Princess Mary Maternity Hospital when 34 weeks pregnant. Her general condition at this time was satisfactory and the pregnancy was progressing normally. She was examined for the second time a fortnight later, but failed to keep an appointment at the 37th week. She lived some distance from Newcastle upon Tyne and attended her own practitioner. Nine days beyond her expected date of delivery the membranes ruptured but she did not come into hospital until labour pains began 2 days later. On admission the foetus was noted to be presenting as a vertex with the greater part of the head still above the pelvic brim. The foetal heart rate was 140 and quite regular, but there was slight meconium staining of the liquor. Frequent strong uterine contractions were occurring. The cervix was three-quarters dilated with a large oedematous anterior lip. Very frequent strong uterine contractions occurred during the next hour and the foetal heart then dropped suddenly to 80 and recovered slowly after each contraction. At the same time thick meconium appeared in the liquor. There had been no descent of the head during this hour and a rectal examination showed the cervical condition to be unchanged.

A lower segment Caesarean section was performed 30 minutes after the slowing of the foetal heart had first been noted. Although the foetal heart was heard strongly at a rate of 80–100 just before the operation started, the the child was stillborn. The lower uterine segment was very vascular and the blood loss was heavier than normal. The placenta was sited completely in the upper uterine segment. A blood transfusion was begun during the operation and 2 pints of blood given. Convalescence was uneventful, the temperature remaining normal until she was discharged from hospital 12 days after operation. Six days later she had a sudden heavy blood loss *per vaginam* and was readmitted to the Princess Mary Maternity Hospital. Her general condition on admission was only fair and a blood transfusion of 2 pints was given. Ergometrine 0.5 mg. was given by intramuscular injection. Her condition improved and the vaginal bleeding ceased. Next day, under a general anaesthetic, the uterus was explored but no placental tissue or membrane was discovered. The uterus was bulky and obviously involuting more slowly than normal. A few small fragments of friable material removed from the site of the scar in the lower uterine segment were reported by the pathologist to be granulation tissue. There was no pyrexia following this exploration of the uterus and no further bleeding took place. The patient was discharged home 4 days later. Blood tests had shown no evidence of any haemor-

rhagic tendency. Heavy vaginal bleeding recurred when the patient was halfway home in the ambulance and she was brought straight back to hospital. The estimated blood loss was 30–40 ounces. Two pints of blood were transfused and once the patient's condition was satisfactory a further exploration of the uterus was carried out under an anaesthetic by a colleague. The previous findings were confirmed but on this occasion the examination caused brisk haemorrhage and the uterus had to be packed. The pack was removed next day. The patient appeared to make satisfactory progress in hospital over the next few days and there was no further blood loss; but 7 days after the second exploration of the uterus, whilst the patient was lying in bed, very heavy bleeding began again and this loss persisted. A blood transfusion was commenced but the patient was obviously losing as much blood *per vaginam* as was being given by transfusion. She was taken to the theatre and, under an anaesthetic, the uterus was packed, but the bleeding was so heavy that blood quickly soaked through the pack and it appeared that hysterectomy was the only means of controlling the blood loss. The operation (subtotal hysterectomy) was technically difficult on account of friability of the tissues and very heavy bleeding. There did not appear to be any significant degree of infection in the lower uterine segment, but examination of the uterus after its removal revealed several large thin-walled sinuses running in the wall of a very thin lower uterine segment; one of these was noted to be ruptured.

During the operation the blood loss was heavy and 5 pints of blood was given by intravenous transfusion. The patient made a satisfactory recovery from this operation and, apart from a slight elevation of temperature on the 10th postoperative day, the convalescent period was uneventful. She was discharged from hospital on 28th January, 1953.

## Comment

It is appreciated that hysterectomy for postpartum haemorrhage is a most unusual procedure but in this case heavy bleeding occurred on 3 occasions within 4 weeks of delivery, and indeed on the last occasion was so severe and persistent that it was not considered justifiable to temporize with further conservative treatment.

The possibility of infection in the lower uterine segment as the cause of the bleeding was considered, but at the time of operation there was no evidence to confirm this suggestion and histological examination of the lower uterine segment, including cross sections of the operation scar, revealed no evidence of infection.

Examination of the specimen suggested that the heavy bleeding had arisen from one or more of the large thin-walled sinuses, which were readily identified on the right postero-lateral aspect of the lower uterine segment, well away from the scar in the anterior wall of the lower segment.

The history of primary postpartum haemorrhage following the delivery of her fourth and fifth babies suggested that some defect in the mechanism of closure of the uterine sinuses had been present at the time of these pregnancies.

I wish to record my thanks to Professor Harvey Evers for permission to publish this case.

FIG. 1
The foetal surface of the placenta.

# MONO-AMNIOTIC TWIN PREGNANCY

BY

JOHN HENDERSON, M.B., M.R.C.O.G.

*Senior Registrar, Raigmore Hospital, Inverness*

THIS is a rare condition, there being only 3 previous cases reported in the British literature (Newman, 1858; Adamson, 1896; Frewer, 1936).

## CASE REPORT

Mrs. A. M., aged 23 years, had had one previous normal pregnancy.

She attended the antenatal clinic of Raigmore Hospital and was admitted at the 38th week when mild pre-eclampsia complicated her twin pregnancy. Both foetuses presented by the vertex. Labour commenced spontaneously at the 40th week and the first infant was delivered, face to pubes, after only 90 minutes. The second twin's cord then prolapsed, tangled with that of the first. It was pulsating vigorously. The first twin's cord was divided between ligatures and the entangled mass of the cords replaced above the second twin's head. An easy forceps delivery was then performed and a vigorous infant obtained. The third stage was uneventful.

The placenta was circular in shape, 9 inches (22 cm.) in diameter and weighed 2 pounds 7 ounces (1.23 kg.). The cords were 40 and 44 inches (100 and 110 cm.) in length respectively and were twisted together through 8 revolutions. They were both of normal thickness and their insertions into the placenta were 2 inches (5 cm.) apart. Numerous anastomoses were present between the vessels on the surface of the placenta. No remnants of an amniotic partition which might have been present between two sacs were present.

The infants weighed 6 pounds 1 ounce (2.9 kg.) and 6 pounds 8 ounces (3.2 kg.) respectively and showed no abnormality. They were breast fed and did well.

This appears to be the first case in the British literature in which both infants survived.

## COMMENT

This subject was fully reviewed in 1935 by Quigley, who collected 109 cases, mostly French and German. The most striking feature of his review was the high rate of foetal loss, which was commonly due to the cords becoming entangled or knotted and then obstructed. The obstruction usually affects the cord of the second twin as that of the first tightens during its delivery. For this reason it is advised that delivery of the second twin be expedited as soon as the diagnosis, which is only possible when the first twin has been born, is made. Cases of miscarriage such as reported by Woodburn (1947) and intrauterine death before labour by Boyle and Richter (1947) have also been due to twisting of the cords.

Coulton, Hertig and Long (1947), when reporting 2 further cases, discussed the development of the condition. The amnion forms after the 7th day and formation of the primitive streak commences about the 13th day. They considered it reasonable to assume that the split in the germ disc takes place between these times, division earlier resulting in the usual uni-ovular twins, later in mono-amniotic monsters.

I am grateful to Dr. A. B. Hay for permission to publish the case and to Mr. C. E. L. Hunt for the photograph.

## REFERENCES

Adamson, —. (1896): *Trans. Edinb. obstet. Soc.*, **22**, 27.

Boyle, J. B., and Richter, C. F. (1947): *Amer. J. Obstet. Gynec.*, **53**, 886.

Coulton, D., Hertig, A. T., and Long, W. N. (1947): *Amer. J. Obstet. Gynec.*, **54**, 119.

Frewer, E. (1936): *Brit. med. J.*, **1**, 159.

Newman, W. (1858): *Edinb. med. J.*, **4**, 8.

Quigley, J. K. (1935): *Amer. J. Obstet. Gynec.*, **29**, 354.

Woodburn, A. (1947): *Ohio St. med. J.*, **43**, 631.

# AMELIA

## Review of the Literature and Report of a Case

BY

L. O. S. POIDEVIN, M.B., B.S., M.R.C.O.G.

*Director of Obstetrics, University of Adelaide*

THE extreme rarity of this congenital anomaly has prompted me to attempt a review of the literature and to report a new case which occurred in my clinic recently at the Queen Victoria Maternity Hospital, Adelaide, South Australia.

The available literature on this subject is somewhat confusing and accurate classification of the condition is made more difficult by the absence of autopsy findings in most of the older reported cases. X-ray evidence also is lacking in most cases.

The classification by Gould (1939) gives 4 grades.

(*a*) *Amelus*: " A monstrosity without limbs."

(*b*) *Phocomelus*: " A monster with rudimentary limbs, the hands and feet being attached almost directly to the trunk."

(*c*) *Ectromelus*: " A single autositic monster characterized by the presence of imperfectly formed limbs."

(*d*) *Hemimelus*: " A monster with incomplete or stunted extremities."

The anatomical extremities include the shoulder girdle and pelvic girdle but no report of absence of the limb girdle bones could be found. Therefore it seems justifiable to apply the term amelia to the monster born with no limb bones whatever beyond the limb girdles.

If this is accepted as the standard of true amelia then several cases already reported as such must be removed from this group and be regarded as phocomelia or ectromelia.

The actual number of true amelias—including the present case—should be reduced to 8 (Table I).

TABLE I

| Author | Number of cases | Sex | Fate |
|---|---|---|---|
| Cholmogoroff | 1 | Male | Stillborn |
| Caesar | 1 | Male | Stillborn |
| Gravely | 1 | Female | Died at 4 weeks |
| Price | 1 | Male | Died at 8 weeks |
| Ilberg | 1 | Female | 3 months foetus |
| Levy | 1 | Female | Stillborn |
| Isenflamm and Rosenmüller | 1 | Male | Stillborn |
| Poidevin | 1 | Male | Stillborn |

It will be noted that the case of Ilberg (1937) is included although it was a non-viable foetus. His report gives full dissection and histological details with a review of the literature but without full references.

### IMPERFECT CASES

The literature can produce scores of cases in this group and no attempt is made here to list them. However, some of those previously claimed as amelia and now removed from that group deserve mention.

Meunier (1897) reviewed a series of cases of mostly imperfect amelias.

Pomerance and Soifer (1949) recently reviewed the literature and reported a case. X-ray investigation of their case showed 3 to 4 cm. of the right humerus and a toe-like appendage in place of the left lower extremity. This is correctly graded as ectromelia.

Of the 12 authors mentioned in their review 4 were not available to me, and of the 8 authors claiming cases of amelia, only 2 can be admitted. Hare's (1858–9) case had portions of both arms present; Slingenberg (1908) gave a full account

of limb developmental abnormalities and mentioned 19 cases, but not one is a true amelia; Price (1928) and Levy (1941) reported the only true amelias. Killingsworth and Engledow (1942) reported a case which had a right lower appendage consisting of fatty tissue and 3 hard bony toe-like structures with nails. Hedenstedt (1944) reported 2 cases of "amelia", the first had the left arm present and the second had the humerus on both sides normally developed. Mooney (1946) reported 1 case with a photograph showing portions of both humeri present. Lukjanow's (1930) case had rudimentary upper ends of both femora present, the right one being 10 millimetres long and the left 12 millmetres.

Courtois *et al.* (1946) reported a case of "amelia" but this had a fragment of the left humerus present and the left lower limb was represented by three metatarsal bones and two phalanges.

Gould and Pyle (1900) report the case of M. Cazotte, otherwise known as Pépin. He died in Paris aged 62 and had no arms, legs or scrotum but from very jutting shoulders on each side were well-formed hands. He was a curiosity often exhibited and was a case of phocomelus. Hastings, in the same publication, reported a child living without any arms or legs, and a reproduction is shown. Reference is also made to this case by Meunier (1897) and it appears that the left lower extremity was rudimentary with some bone and a terminal nail so that it cannot be classed as amelia.

## Report of a Recent Case

Case No. 2269. Mrs. M. K., gravida-3, was born in Germany. She was married in September 1948, when 27 years of age. Her first pregnancy in 1949 terminated in a miscarriage at 3 months, and her second in 1951 in an operation for ectopic tubal gestation.

There was no family history of developmental defects on either side and she stated that both she and her husband were in good health when she conceived, following her last menstrual period on 4th April, 1952.

She had rheumatic fever when 17 years of age but gave no evidence of cardiac failure when first seen on 30th June, 1952, and appeared in good health. Routine chest X-ray showed no abnormality; haemoglobin was 90 per cent, Wassermann reaction negative and her blood group was $O_1$ Rh positive.

On 26th August, 1952, the patient appeared worried about her "heart condition" and complained of dyspnoea. She was admitted to hospital for observation. There was an apical systolic murmur present and a normal pulse rate and blood-pressure, and after 4 days she was allowed home. Her cardio-vascular system was considered normal.

Subsequent antenatal examinations were quite satisfactory and the pregnancy proceeded uneventfully. At no stage did she suffer any known infectious illness or trauma. Her diet was adequate and her weight gain from June, 1952, until January 1953, was 7 pounds.

On 7th August, 1952, she stated she felt foetal movements and she continued to do so throughout the pregnancy. On retrograde questioning she did not recall kicks, but had rolling movements. The foetal heart was always heard and the lie was longitudinal, most often in the left-occipito-anterior position. A foetal X-ray was never considered necessary by those who examined her.

### *Labour*

The first stage was slow and ineffective in the early period but by 9 a.m. on 13th January, 1953, it was well established with the cervix three-quarters dilated. The foetus was in left-occipito-anterior position with a heart rate regular and 140 per minute. She was given 100 mg. pethidine.

Two hours later the foetal heart rate suddenly became slow and irregular during descent and a forceps delivery was decided upon. This was easily effected through a fully dilated cervix. The baby was a male amelia which never attempted to breathe (Fig. 1).

The third stage of labour was normal and followed by a normal puerperium, except that lactation was artificially suppressed.

## Autopsy Report

*External Examination*

A male child weighing 4 pounds, with head circumference 13¼ inches (33 cm.) and sitting height 25 cm.

There is no evidence of any limbs except for a small button of skin at the site of the base of the left lower limb; a small dimple is present in the corresponding position on the right side. The anus is much stenosed, admitting the end of a match. The scrotum is empty. The nose is deviated markedly to the left.

*Internal Examination*

*Limb Girdles.* Normal looking clavicles and scapulae are present except that the latter have no glenoid cavity.

The ischium is absent on the right side (Fig. 2) and there are no acetabula present. The musculature attached to the limb girdles is poorly developed; some of the larger muscles such as the trapezius and latissimus dorsi are readily recognized, but most other muscles are not evident in a mass of fibrous tissue and fat. The subclavian arteries seem normal at their origin but they narrow down suddenly and become lost as they approach the limb bases. The external iliac and femoral arteries are present but the latter are very narrow and soon disappear.

*Nervous system*

The brain is normal.

The spinal cord is of normal length with cervical and lumbo-sacral swellings present (Fig. 3). Nerve roots and nerves which normally go to make up the brachial and lumbo-sacral plexuses are definitely smaller than normal and no definite plexuses are present. Nerves of supply to the trunk in the region of the limb bases (e.g., spinal accessory and subcostal) appear normal. On section the cord shows a much enlarged central canal extending from the sixth cervical to the twelfth thoracic segment, gradually tapering to its lower limit. (Detailed microscopic examination of the cord will be reported elsewhere.)

*Thoracic and Abdominal Contents*

The diaphragm is deficient in its left half. The part of the diaphragm present is membranous except for the crura which are well developed and muscular. The greater part of the alimentary canal and associated organs are present in the left side of the thorax (these include the gut from stomach to transverse colon, the pancreas, part of the spleen and part of the liver which is notched near its middle by the free edge of the diaphragm).

The heart is displaced well over to the right and the left lung is very poorly developed. The trachea and main bronchi are normal but the left bronchus narrows abruptly and stops at the vestigial left lung. The right lung is smaller than normal and the lobes are incompletely separated.

The heart is small and shows several abnormalities: enlarged right atrium and right ventricle: complete dextroposition of the aorta which arises from the right ventricle: the left ventricle is much smaller than the right, the pulmonary artery arises from it: there is a large deficiency of the upper part of the interventricular septum: the foramen ovale is normal except for fenestration of the septum primum: the ductus arteriosus has a thin wall and is widely patent.

The spleen is in two parts: a tiny spleen situated in the thorax just below the pancreas and a separate elongated narrow part extending from the lower part of the thorax down the left side of the abdomen with its lower end fused with the left testis.

The testes are situated at the internal rings.

The kidneys and adrenals are situated lower than usual and reach to the pelvic brim. The adrenals are only half the normal size.

The large intestine below the splenic flexure is markedly distended with meconium.

The thymus is normal (weight 11 g.)

The placenta is small (weight 8¼ ounces). No macroscopic abnormality of placenta or membranes is apparent.

## Commentary

The cause of such developmental anomalies must at present remain purely conjectural. Older theories involving amniotic bands are not admissible today.

For over 100 years it has been known that experimental interference—either traumatic, toxic or environmental—can produce foetal abnormalities. Such factors, in a gross form at least, seem to be excluded here. Maternal infection too appears to be unlikely. In view of the earlier obstetrical history the possibility of an adverse maternal environment cannot be completely ignored.

The other major factor in producing such abnormalities is genetic. This may have operated alone or in conjunction with maternal insufficiency. Further than that it is not possible to go.

## Summary

(1) A case of what is considered "true" amelia is presented.

(2) Survey of the literature describes only 7 other cases of this grade.

(3) The cause in the present case appears to be mainly genetic.

My thanks are due to Dr. Dudley Packer, Honorary Anatomist to the Queen Victoria Maternity Hospital, for performing and reporting on the autopsy.

I also wish to thank Miss G. D. Walsh of the Department of Anatomy, University of Adelaide, for the photography.

FIG. 1
The Author's case as delivered.

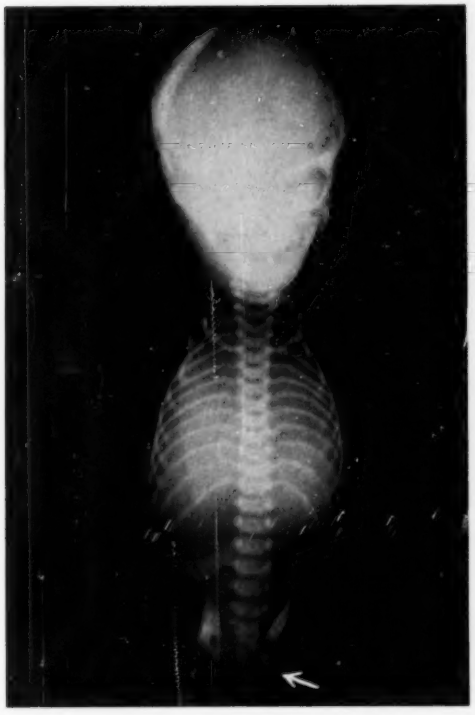


FIG. 2
The right ischium is absent. Arrow indicates left ischium.

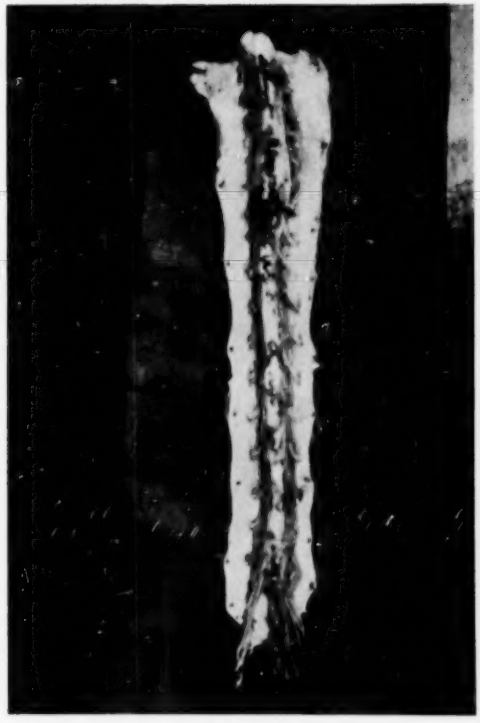


FIG. 3
The Spinal Cord.

## References


Caesar, R. T. (1889): *Brit. med. J.*, **1**, 525.

Cholmogoroff, S. (1888): *Zbl. Gynäk.*, **12**, 819.

Courtois, J., Lelièvre, and Brière (1946): *Gynéc. Obstét.*, **45**, 122.

Gould, G. M. (1939): *Medical dictionary*. 4th edition. Edited by R. J. E. Scott and C. V. Brownlee. Lewis, London.

Gould, G. M., and Pyle, W. L. (1900): *Anomalies and curiosities of medicine*. Popular edition. Saunders, Philadelphia. p. 263.

Gravely, H. (1889): *Brit. med. J.*, **1**, 1289.

Hare (1858–9): *Trans. path. Soc., Lond.*, **10**, 308.

Hastings (*Quoted from* Gould and Pyle (1900).)

Hedenstedt, S. (1944): *Acta obstet. gynec. scand.*, **24**, 271.

Ilberg, G. (1937): *Z. Geburtsh. Gynäk.*, **114**, 174.

Isenflamm, H. F., and Rosenmüller, J. C. (1800): *Beiträge für die Zergliederungskunst. Leipzig.* Bd. I, Taf. 1, Fig. 2, p. 268.

Killingsworth, P. W., and Engledow, R. (1942): *Amer. J. Dis. Child.*, **63**, 914.

Levy, J. L. (1941): *Sth. med. J.*, **34**, 1085.

Lukjanow, G. N. (1930): *Z. ges. Anat., Abt. I*, **93**, 645.

Meunier, H. (1897): *Nouvelle Iconographie de la Salpêtrière*. Paris. Tome 10, 15.

Mooney, V. (1946): *Pennsylvania med. J.*, **49**, 736.

Pomerance, H. H., and Soifer, H. (1949): *J. Pediat.* **34**, 465.

Price, M. D. (1928): *J. Indiana st. med. Ass.*, **21**, 250

Slingenberg, B. (1908): *Virchows Arch.*, **193**, 1.

Warkany, J., Nelson, R. C., and Schraffenberger, E. (1943): *J. Bone Jt Surg.*, **25**, 261.

# Obituary

## JAMES MONTAGU WYATT

1883—1953

JAMES WYATT died at St. Thomas's Hospital on 31st July, 1953. His health had not been good for a few years but his final illness lasted only a few days.

He was born at 20 Queen Square on 21st April, 1883, the fifth son of Thomas Henry Wyatt, M.V.O., chief civil assistant to the Quartermaster-General. He came of a family that has had in it several generations of distinguished architects. His grandfather, Thomas Henry Wyatt, did a great deal of building and alterations of hospitals including the Middlesex, St. Mary's, the Brompton, and the Cancer Hospitals. In this work he was helped by advice given him by Florence Nightingale. A great-uncle, Sir Matthew Digby Wyatt, was joint architect of the great Exhibition of 1851. He was related to many other architects including James Wyatt, President of the Royal Academy.

He was educated at Merchant Taylors' School and from there went to St. Thomas's Hospital Medical School in 1900. He was a prominent student and won the Midwifery and Gynaecological prizes. He qualified M.R.C.S., L.R.C.P. in 1905 and was appointed junior and senior obstetric house physician to Drs. Tate and Fairbairn.

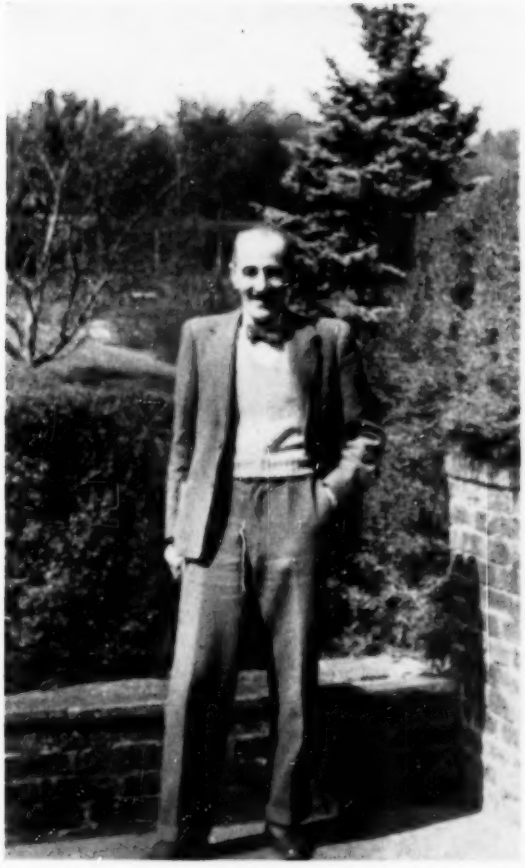
After finishing his house appointments he went to China and spent two years or more working in Shanghai with two of his old St. Thomas's friends who practised there. But as his great interest in medicine was obstetrics and gynaecology he returned to London to work for the F.R.C.S. and the London M.B., B.S., which he took in 1911 and the fellowship in 1910.

He then settled down to fit himself to become a consultant in obstetrics and gynaecology. After being R.M.O. at Queen Charlotte's Hospital he was appointed Obstetric Tutor and Registrar at St. Thomas's.

While holding this appointment the 1914 war came and in the very early days of it he went to Brussels in charge of a Red Cross unit. His unit was soon in the hands of the Germans who after some weeks allowed it to return to England. After much negotiation Wyatt got all his people into a train for home but even then his troubles were not over. As the train was moving out of the station watched by a number of German officials one of the nurses put her head out of a window and cocked a snook at them. Naturally the train was stopped at the next station. Wyatt got out to show his papers and was met by a very angry officer. When Wyatt presented the papers for inspection the officer knocked them out of his hands and scattered them all over the platform. When the officer explained the cause of his anger James was able to persuade him that the nurse was simply waving good-bye and in some little time the train was allowed to go on.

He got back to St. Thomas's in October 1914 where in the next few months the 5th London General Hospital was established. He was appointed to its staff as Captain R.A.M.C.T. where, like other members of the St. Thomas's staff who were still in London, he did the work of the military hospital as well as the civil work of St. Thomas's and the teaching of students.

Besides all this he did most splendid and devoted work in charge of Lady Ridley's hospital for officers in Carlton House Terrace. He visited it early in the mornings and spent many hours there every evening, working until late at night, and made it one of the best, if not the best,



JAMES MONTAGU WYATT

of the many hospitals of this type in London. Late in the war he was ordered abroad.

But for the war, during which no appointments were made to the staff, he would certainly have been put on when Dr. Walter Tate died in 1916.

At the end of the war he was appointed to the staff as the third obstetric physician. He was very active and quickly developed a large antenatal clinic which had been started some years before but had had to remain comparatively small on account of war difficulties.

He conceived the idea of supervising the newborn and giving advice to their mothers after leaving the maternity wards and to him is due the credit of starting the now world-wide organized care of infants. The first Baby Clinic in this or any other county as far as I can discover was established by Wyatt at St. Thomas's Hospital. It soon became very large and he took charge of it for many years until it was transferred to the Children's Department.

He never spared himself and was most conscientious in all his duties at the hospital. He was a first-rate teacher and operator and had excellent clinical judgment. He soon had a large private practice but it was never allowed to interfere with his hospital work. He was gynaecological surgeon to the Grosvenor Hospital and until the end of his life took a very active part in the management and development of the hospital.

He was a born manager, he knew his own mind as to what should be done and was prepared to fight for it. He took the utmost pains to have his facts and arguments ready to present at the meetings of the hospital staffs.

He was in charge of the Puerperal Unit at Hampstead before it was taken over by the London County Council but continued under the L.C.C. until the outbreak of war in 1939. He became an authority on puerperal infection and wrote and spoke many times on different aspects of this subject. Among other subjects on which he wrote were Toxaemia of Pregnancy and Treatment of Cancer.

He was prominent in the early discussions that took place before the foundation of the College of Obstetricians and Gynaecologists in 1929 and was one of the foundation fellows. He served on the Council from 1941 to 1946 and was vice-president of the College from 1946 to 1949. He was also a member of the Fellowship Selection Committee and of the Examination Committee, of which he was chairman from 1947 until 1949.

He was an active member of the section of Obstetrics and Gynaecology of the Royal Society of Medicine and regularly attended its meetings. He read many papers and was a frequent contributor to the discussions. He was secretary of the Section for two years and President 1946–7. For many years he was chairman of the Children's Sanatorium at Holt in Norfolk.

He was Examiner in Midwifery and Diseases of Women to the Universities of Oxford, Cambridge, London, and Manchester, and the Conjoint Board, and served many years as examiner to the Central Midwives Board.

He took a leading part in the arrangements for the evacuation of the Medical School of St. Thomas's in the early part of the second world war and became warden of the students' hostel established at Manor House, Godalming. It was in no small measure due to him that the transfer of the School and its later management were so great a success. On the return of the School to London in 1946 Wyatt left the staff of the hospital three years after the normal retiring age.

After this he put in a great deal of hard work as a member of the governing body of St. Thomas's and of Queen Charlotte's and the Chelsea Hospital for Women. Perhaps Wyatt's outstanding characteristic was his unbounded enthusiasm which was apparent in all he did and said. It lasted to the end of his life in spite of serious asthma that afflicted him in his last few years and added much to the burden of the numerous activities he took upon himself after his retirement from the St. Thomas's staff. His energy seemed to be as unbounded as his enthusiasm.

He became a member of the Central Midwives Board in 1947 and served until 1952. It was clear to its members at their meetings that he had always mastered the details of the problems on the agenda which were frequently long and complicated and usually had valuable criticisms

to offer; occasionally these were submitted in writing if he could not for any reason attend the meeting.

In 1948, on the formation of the South-west Metropolitan Regional Board, which covered an area from London to the South Coast, he became a member of it and was most energetic in his duties which involved numerous journeys for meetings and inspections in distant parts of the Region. The Regional Board was, I think, his greatest interest from its formation until his death. He had a profound knowledge of the working of the hospital side of the Health Service and did his utmost to make it a success. Besides all his activities he served on many committees in connection with the health service.

Soon after joining the School James became a prominent figure at St. Thomas's. He got into the Rugby side his first season and played regularly for five years; he was an energetic, courageous forward. He was a good organizer and would manage anything connected with the hospital and school—dinners, dances, sports, etc.—and did it exceedingly well. For many years he was president of the hospital rugby football club, seldom missed a match, and watched over the teams with a fatherly interest. For some years the hospital side has toured the south-west of England based in Mevagissey where James had a charming house, and there he entertained in a most delightful way. Many have very pleasant memories of these tours and the hospitality at the Watch House.

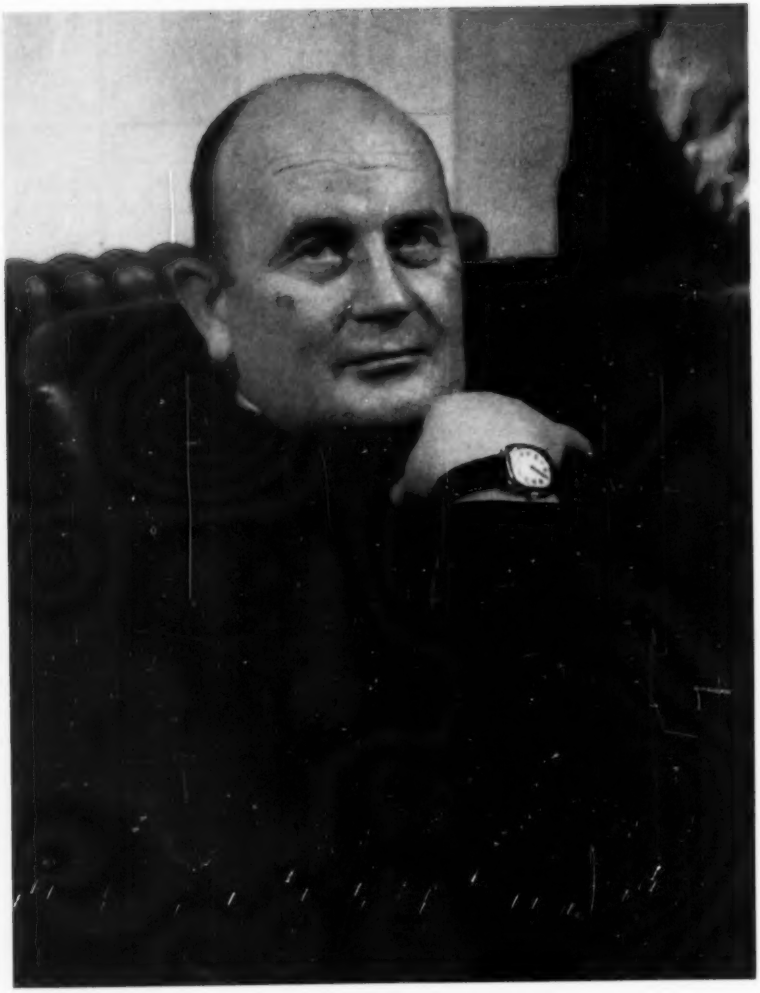
He was an enthusiastic supporter of amateur boxing, though I believe never a great boxer himself, and had the great distinction of being President of the Amateur Boxing Association for 10 years. He took a considerable part in the preliminary organization for the Olympic Games at Wembley in 1948.

He had a jaunty walk and I often felt as I saw him going round the hospital that he would break into a run at any moment.

He had one hobby that was particularly pleasing to his friends: he was an extremely good cook, loved cooking and took a keen interest in it. He could produce a wonderful dinner. As warden at Manor House on several occasions when the cook had failed to turn up he produced a first-rate meal for the students there.

James Wyatt was kind and considerate to all, willingly helpful to those who sought his advice in their difficulties and very generous to many. He was a member of a large and united family. He never married but his multifarious interests seemed to take the place of a family life, he was cheerful and gay, was " in everything ", and had a host of friends.

J. P. HEDLEY



WALTER NETLEY SEARLE

# Obituary

## WALTER NETLEY SEARLE

1904—1953

WALTER NETLEY SEARLE, Surgeon to Outpatients at the Chelsea Hospital for Women and Obstetric Surgeon and Lecturer in Obstetrics and Gynaecology at Westminster Hospital, died on 30th August at the age of 49. He was on a health visit to New Zealand and, while it had been known for the past several years that his health had been failing, his death on the voyage was unexpected.

Walter Searle was born in Oamaru in the South Island of New Zealand in 1904 and received his education at the Waitaki Boys' High School and at the University of Otago Medical School, Dunedin. He graduated M.B., Ch.B. in 1929. After graduation he held house appointments in New Zealand and then proceeded to Scotland where he served as Resident Obstetric Officer at the Royal Maternity and Women's Hospital in Glasgow. From there he proceeded to London, where he was House Surgeon, and later Resident Medical Officer at the Chelsea Hospital for Women. The quality of his work was recognized by his appointment as Registrar and Radium Officer to the Chelsea Hospital for Women, and later to the office of Obstetrical and Gynaecological Registrar and Tutor to Westminster Hospital and Medical School. During this time he obtained the F.R.C.S.(Ed.) in 1931, the M.R.C.O.G. in 1933 and the F.R.C.S.(Eng.) in 1937.

His two registrarships subsequently led to his election to the honorary staffs of both the Chelsea Hospital for Women and Westminster Hospital and Medical School, and he also became Consultant Obstetrician to the Borough of Enfield and Gynaecological Surgeon to the East Ham Memorial Hospital. He was elected F.R.C.O.G. in 1948 and had held examinerships for the Royal College of Obstetricians and Gynaecologists, the Central Midwives Board, and the Society of Apothecaries.

In his young days Searle was a most useful all-round cricketer and he retained his interest in the game to the end.

His many friends were distressed over the last three or four years to recognize a deterioration in his health, which appeared to originate in an obscure cardiac lesion, but most of us who knew him well always remember his high professional attainments and his extremely human qualities of companionship, kindliness and friendliness. He exhibited a great interest in antiques and was never happier than when on holiday with his family on the Isle of Arran.

He married the daughter of Professor R. J. T. Bell, who formerly held the chair of mathematics at Otago University. One son survives him. To his widow goes the admiration of all friends for the loyalty, courage and devotion which she showed during his long illness.

CHARLES W. READ

# Obituary

## EWEN JOHN MACLEAN

1865—1953

THE death of Sir Ewen Maclean in Cardiff on 13th October, a few days before his 88th birthday, removes from our midst a man of remarkable ability and of the highest achievements who in his day and generation wielded much authority and influence.

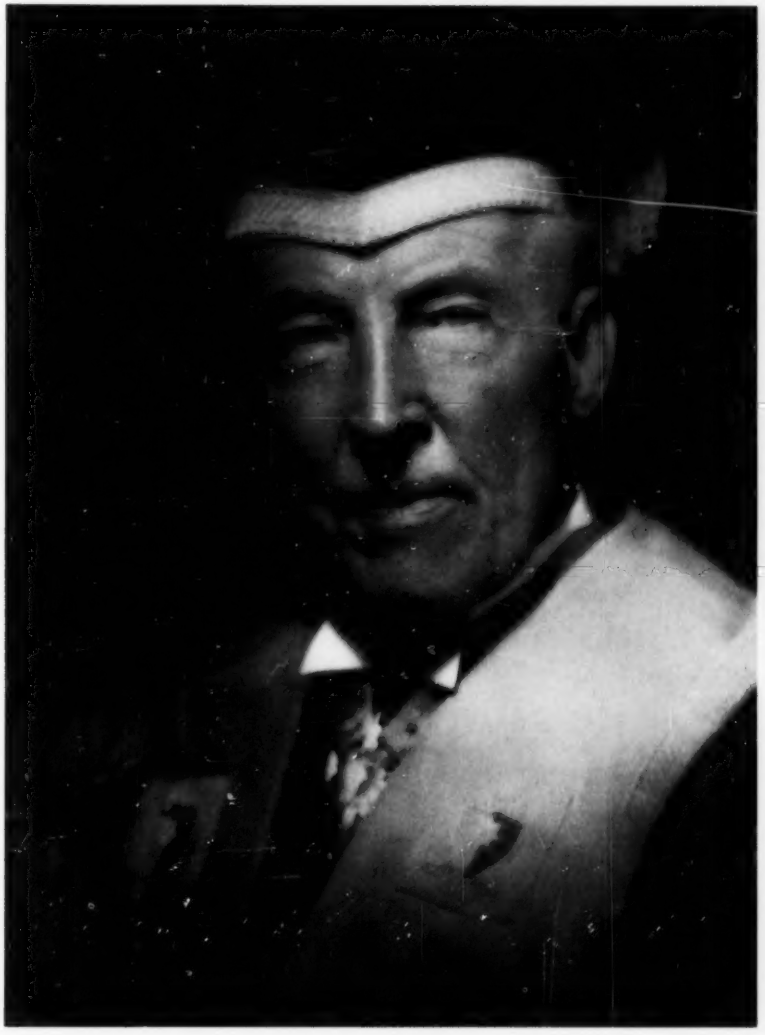
His parents were Highland and Gaelic-speaking; they came to live in Carmarthen where young Ewen was educated in the Grammar School as well as at Haverfordwest.

Later he went to Edinburgh University where he graduated M.B., C.M. with honours in 1889, and later M.D., also with honours, in 1891. He subsequently became M.R.C.P., and in 1922 he was elected a Fellow, while he had become a Fellow of the Royal Society of Edinburgh in 1899. After serving a period as House Surgeon in the Bristol Hospital for Women and Children he started his life's work when he was appointed Registrar at the Chelsea Hospital for Women.

On the death of John Williams in 1901, Ewen Maclean was appointed senior obstetrician and gynaecologist to Cardiff Royal Infirmary and, when the Welsh National School of Medicine was created in the University of Wales in 1921, he became the first Professor of Obstetrics and Gynaecology. Both of these appointments he held with distinction until 1931 when he retired with consulting and emeritus status. He was examiner in obstetrics and gynaecology to the Conjoint Board and also to the Universities of Bristol and of Liverpool. His contributions to the literature of his speciality, while not numerous, were always sound and of considerable clinical value. They included papers on elephantiasis of the vulva and the late effects of puerperal sepsis, while he wrote the section on "Tuberculous Infection of the Female Genitalia" in the *Encyclopaedia of Midwifery and Diseases of Women* published in 1921.

He was a keen clinician, a conscientious and conservative surgeon and a teacher of marked ability, while his wide experience of men and things formed an important background to his vast clinical experience. His local professsional reputation was of the highest so that, in spite of his many administrative commitments, he built up a very large consulting practice in South Wales.

But it was particularly in committee and council work that Sir Ewen excelled, and in these capacities he was in great demand. He was for many years a member of the Medical Advisory Committee of the Ministry of Health and Chairman of the Welsh Consultative Council. His services to the British Medical Association were outstanding. Locally he occupied the position of Chairman of the Cardiff Division, President of the South Wales and Monmouthshire Branch, Chairman of the Welsh Committee, and Chairman of the Contract Practice Committee. Centrally, he was a Member of Council and Chairman of the Representative Body in the stormy days of 1911 when Lloyd George's National Health Insurance Act was being so hotly debated, and the line of action that he then advised was what was subsequently adopted by the profession. When the Annual Meeting of the Association was held in Cardiff in 1928 Sir Ewen was elected President, and for a number of years afterwards he retained a seat on the Council. At the Glasgow Meeting of the B.M.A. in 1922 he was President of the Section of Obstetrics and Gynaecology, while he was



EWEN JOHN MACLEAN

later President of the same section in the Royal Society of Medicine.

The Royal College of Obstetricians and Gynaecologists owes much to Sir Ewen. He was one of the small band of pioneers who first explored the possibility of the formation of such an institution. He was one of the founders, an original member of the Council and a Foundation Fellow. In its early days the college passed through a very difficult and critical period and at that time a move in the wrong direction could have proved disastrous and could even have resulted in the institution being wrecked. At this stage Sir Ewen's calm assessment of the factors concerned, his long-headed and sagacious advice, and his infinite patience, were of the greatest value, and on more than one occasion averted a dangerous crisis.

He was President of the College from 1935 to 1938 and during that period his main efforts were directed to the obtaining of a Royal Charter for the College. This, in fact, was granted, but not until 1947, being delayed by the war years. In that year, and on the occasion of the granting of the Royal Charter, the Honorary Fellowship of the College was conferred on Sir Ewen and the other surviving founders. He remained a member of the College Council for some years after his presidency, but a severe heart attack in 1943 materially curtailed his activities and particularly his journeys to London.

In the first World War Sir Ewen was Adjutant to the 3rd Western General Hospital, Cardiff, with the rank of Major, R.A.M.C. (T.F.), while in 1917 and 1918 he was O.C. Eaton Hall Officers' Hospital, Chester, with the rank of Lieutenant-Colonel, and he later commanded the 3rd Western General Hospital.

Maclean was a bachelor and the younger brother of Sir Donald Maclean, who, at the time of his death in 1932, was President of the Board of Education under Mr. Stanley Baldwin. His sister, Miss Agnes Maclean, has devoted the recent years almost entirely to the sedulous care of her brother in his failing health, and the deep sympathy of many friends is extended to her.

Sir Ewen was the recipient of many honours. He was a Justice of the Peace for the City of Cardiff and a Deputy Lieutenant of the County of Glamorgan. The University of Edinburgh conferred on him the honorary degree of Doctor of Laws in 1933 as did the University of Wales in 1947, while he received from Manchester University the Honorary Doctorate of Science in 1929. The American College of Surgeons elected him to its honorary fellowship in 1927, and in 1935 he received the Honorary M.D. from Melbourne University. Finally, in 1923 his late Majesty, King George V, conferred on him the honour of Knight Bachelor.

In appearance tall, slim and distinguished, and in personality the most courteous and approachable of men, with a quick wit and a keen sense of humour, Sir Ewen was a most acceptable member of any gathering. A most accomplished speaker, he was much in demand in this capacity. The completion of Sir Ewen's life of accomplishment severs one of the few remaining links with the old school of which he was such an ornament. His personality, his character and his achievements could be viewed from many angles: for my part, I shall always remember him as a dear and loyal colleague with whom I worked in the closest harmony for many happy years.

GILBERT I. STRACHAN

## ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of Council was held at the College House on Friday, 16th October, 1953, with the President, Mr. Arthur A. Gemmell, in the Chair.

The following were admitted to the Membership:

Louis Julius Abramowitz
Subrahmanyan Alankaram
William John Ronald Anderson
Geoffrey Spencer Andrew
Amiya Kumar Bose
John Charles Brace
Timothy John Buckley
Samuel Burke
Robert Keltie Burt
James Grant Cameron
Rory Shaun Casement
Po Wong Christina Chow
Maureen Daly Connolly
Robert Logan Edwards
Michael Brendan Flanagan
Frank Menzies Cameron Forster
Kathleen May Frith
Michael Cameron Gordon Grant
Peter Brutus Guastalla
Reginald Henry James Hamlin
John William Simmons Harris
Joseph Masters Holmes
Cyrus Arvon Jones
Rees Lloyd Jones
Ian Ross Macdonald
Betty Mallace
Gerald Arthur Manly
Donald Norwood Menzies
Maurice Cecil Michelow
John Joseph Nattrass
Hugh Hyman Neifeld
Francois Nicolas Neser
James Patrick O'Dwyer
Dharma Rau Patnaik
Clara Phillips
Basil George Pickles
William Rotheram
James Steel Scott
James Marshall Stewart
Ronald Anderson Struthers
Valerie Mary Thompson
Cyril Joseph Thornberry
Harry Ulman
Chester Gilmore Wilson

## NICHOLS FELLOWSHIP

A Grant of £225 will be awarded for one year, with the possibility of an extension for a second year, by the Council of the Royal Society of Medicine, in aid of research to advance knowledge in obstetrics and gynaecology.

Applications giving an outline of the proposed research and place at which it will be carried out should reach the Secretary, Royal Society of Medicine, 1 Wimpole Street, London, W.1, by 15th May, 1954.

# REPORTS OF SOCIETIES

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

MARCH, 1953

A Meeting of the North of England Obstetrical and Gynaecological Society was held in the Institute of Pathology, Leeds, on Friday, 27th March, 1953. The President, Mr. D. Currie, was in the Chair.

Dr. A. V. C. Bibby described

### TWO CASES OF RUPTURED UTERUS IN ACCIDENTAL HAEMORRHAGE

Dr. Bibby remarked that incomplete rupture in accidental haemorrhage had quite often been reported, but he had traced reports of only 2 other cases of complete rupture in this condition—by Gibberd and Gwillim in 1933. Gibberd's case had a fatal outcome, but Gwillim's recovered. Both the cases to be described ended fatally and all 4 were treated by hysterectomy.

*The first case* was of a woman admitted to Leeds Maternity Hospital in 1939 under Mrs. Adamson. She was aged 32 and had had 4 previous pregnancies, the first 3 of which had been normal. During the 4th pregnancy there had been a severe anaemia requiring blood transfusion, and, before the delivery of a stillborn, premature child, there had been mild antepartum haemorrhage.

Apart from some severe vomiting early on, the 5th pregnancy had been normal until she was admitted late in the 7th month with moderately severe vaginal bleeding. Her general condition gave rise to no anxiety but no foetal parts could be felt, and no foetal heart was heard. The cervix was closed, and, to control the bleeding, the membranes were ruptured and a vaginal pack was inserted. A blood transfusion was given but there was no recurrence of the bleeding in spite of the pack being pushed out in 4 hours. More than 12 hours later, and in the presence of a strongly contracting uterus, there was no sign of dilatation of the cervix, the fundus had risen by 3 fingers' breadth, and the patient's general condition was deteriorating. At abdominal section it was found that the whole of the uterine wall was infiltrated with blood, and that there was a rupture low down posteriorly through which the foetus was extruded during manipulation.

Total hysterectomy was performed and the patient's condition at the end of the operation was satisfactory.

She lived for 12 days after this with an oliguria and a steadily rising blood urea. As she was found to be very anaemic on the 5th post-operative day, she was given a further blood transfusion to which she had a severe reaction.

The cervix was examined microscopically because it was considered to be a contributory cause of the rupture. It was reported as containing "much increased fibrous tissue."

The postmortem report stated that there was a subacute nephritis, cloudy swelling of the liver, and toxic changes in all organs.

*The second case* was a gravida-5, aged 37, who was admitted to the Leeds Maternity Hospital under Mr. Jeaffreson in 1951. She had had 2 normal full-time births and 2 abortions previously. With the 5th pregnancy she threatened to abort at 4½ months, and then was quite well until, at 32 weeks and 12 hours before admission, she was seized with abdominal pain. She was thought to be in labour but 8 hours later began to bleed, and, as both this and the pain continued and became more severe, she was sent into hospital.

On admission she was still bleeding steadily but her general condition was good, and her blood-pressure was 110/70. There was slight tenderness of the uterus, but it was contracting and relaxing well. The presentation was felt to be a breech but no foetal heart could be heard.

Vaginally the cervix was not taken up but admitted 2 fingers. There was an intact bag of membranes but he felt what was thought to be the internal os. As the bleeding was still continuing a low rupture of the membranes was carried out, and, when this failed to staunch the blood, a foot which was lying just over the os was drawn down into the vagina. This effectively controlled the bleeding. As the systolic blood-pressure had dropped to 90, a blood transfusion was started.

During the next 3 hours the patient's general condition remained good, labour progressed and the abdominal signs did not alter. At the end of this time she delivered herself of a 4 pound 2 ounce stillborn child followed by a steady loss of dark altered blood. Within 15 minutes the placenta was born with no accompanying blood clot but with a considerable quantity of dark blood and the uterus retracted well. The blood transfusion was continued because the blood-pressure was still only 90/55.

Half an hour later bleeding recommenced and increased rapidly until the patient collapsed. Several pints of blood were quickly given, and an exploration of the uterus under anaesthesia showed there to be a complete rupture posteriorly, 2 inches long, at about the level of the junction of the upper and lower segments, but not involving the cervix. The uterus was still quite firm.

At abdominal section the uterus was a deep plum colour—almost black. There were huge retroperi-

toneal haemorrhages involving both broad ligaments and extending widely on the posterior abdominal wall, and some free blood-stained fluid in the peritoneal cavity. The rupture extended through all coats, and the uterine muscle was very friable.

Sub-total hysterectomy was performed. It was difficult to secure haemostasis owing to the condition of the tissues. After the operation the patient rallied slightly but then, in spite of massive blood transfusion, became more and more shocked. Marked cyanosis, unrelieved by oxygen, was a feature of the 3 hours after operation before she died.

Postmortem examination confirmed the gross retroperitoneal haemorrhage, and showed acute haemorrhagic lesions of the kidneys and a severe toxic change throughout the liver.

*Comment*

In the notes of the first case, much was made of the condition of the cervix, and the microscopical finding of increased fibrous tissue lent weight to the diagnosis of stenosis of the cervix made at the time. His own feeling was that this was probably not a pathological cervix functionally or anatomically.

He had no doubt that the second woman had a placenta praevia, but this would be discounted in relation to the rupture, because the placenta was on the anterior wall and the rupture occurred posteriorly.

In Gibberd's case, during observation in the ward, the foetus dramatically escaped into the peritoneal cavity through a large fundal rupture. He considered that the rupture was the result of a sudden increase in intra-uterine bleeding, but made no observation about the state of the uterine wall except that it was thin.

In Gwillim's case there was again a sudden and dramatic rupture which occurred at full dilatation, and he remarked that there were interstitial haemorrhages in all the coats of the uterus.

In these 2 cases, where there were very large rents in the uterus and the foetus had escaped, hysterectomy was the only possible treatment. But with the second of his own 2 cases perhaps intra-uterine packing might have been better.

*Discussion*

The President wanted to know why the uterus had not contracted to squeeze out blood until the baby had been delivered.

Miss E. Peaker said that she was the registrar at the time of the first case and she considered that there was definite pathological stenosis of the cervix. Rupture was due to the strong contractions and death was due to the transfusion reaction.

Dr. D. C. J. Dewhurst reminded the Society of 2 cases of rupture of the lower segment scar which he had reported to them. This had taught him that the uterus might well continue to contract after rupture.

Mr. D. C. Racker thought that rupture might occur through the scar of an incomplete small tear sustained in a previous labour. Section of the area of the tear might prove that this was so.

Dr. G. Manley described

A Case of Carcinoma of the Vulva

The patient presented a sorry picture when first seen in October 1952. She was aged 52 years and, over the last 18 months, had noticed a lump in the vulval region, gradually increasing in size until it was as large as an orange. The lump became infected, bled easily, and was extremely malodorous. In addition, she had myasthenia gravis, for which she was receiving, with beneficial effect, prostigmine mg. 15 t.i.d.

Sometime before coming to Park Hospital she had been advised against operation at another centre, and even the benefits of irradiation therapy had been denied her, for she was told that the disease was too far advanced.

She was an exsanguinated middle-aged lady in a smelly state due to secondary infection and necrosis from a large, fungating, tender, polypoidal vulval carcinoma. This lesion spread down to near the anal canal and outwards over the right labia and upwards over the mons. It was at least the size of an orange and blocked the vaginal orifice so completely that examination at this stage to determine urethral involvement was impossible.

On general examination, apart from her anaemia, there were no abnormal findings—the inguinal nodes were not palpable, there was no dependent oedema, the liver was not enlarged, and there were no clinical or X-ray signs of pulmonary metastases. Her haemoglobin was 19 per cent and the red-cell count was 1½ millions. There was no bony destruction in the pubes. Pyelography revealed good kidney function and a bladder normal in outline.

The treatment was divided into four main parts:—

*Firstly*, following repeated blood transfusions on the 13th October, 1952, a vulvectomy was performed. The tumour was mainly on the right side, but extended widely out towards the groin. The urethral orifice and the vagina were not involved. To ensure adequate removal, apparently healthy tissue at least 1 inch lateral to the growth was excised, resulting in a large open space, the edges of which could not be brought together, even with undercutting and small relaxing incisions. Due to her poor general condition, the presence of myasthenia gravis, and the large size of the growth it was decided to perform lymphadenectomy at a second operation. The large space was thus allowed to granulate. The histological report on the tumour was "a well differentiated squamous cell carcinoma".

Her *second* operation was performed 16 days later, when a bilateral block dissection of the inguinal and external iliac nodes was performed through large incisions extending from above Poupart's ligament

downwards, parallel to the sartorius muscle, to near the apex of the femoral triangle. Cloquet's node was present on the left, but not on the right side. The wounds were closed with small drains. There was no histological evidence of malignancy in any of the nodes excised.

At the same operation, a double-barrelled transverse colostomy was made, as it was felt that healing of the bare area about the vagina would progress more satisfactorily in the absence of faecal contamination.

The colostomy was opened the next day and was functioning well on her leaving hospital. The vulval region granulated and remained clean; the incision in the left groin healed by primary intention, but the right-sided wound broke down completely, and the bridge of skin between vulva and the incision sloughed resulting in a very large area uncovered by skin.

Her *fourth* operation was performed 1 month after her original vulvectomy, when she was transferred to another hospital for skin grafting by split skin graft taken from the thighs. She was eventually sent home for New Year, her total stay in the two hospitals being 11 weeks. The grafts had taken well and all wounds had healed cleanly.

In spite of an attack of influenza in the recent past which confined her to bed, she had been remarkably well and able to get about the house, something which she was unable to do before the operation.

In conclusion Dr. Manley said that this case was presented not because of its rarity, but simply to show that seemingly inoperable vulval cancers could be subjected to operation and even if not cured, at least life could be made happier, for she could now go about without the putrid stench of a really foul, fungating cancer.

*Discussion*

The President doubted whether the enormous radical operation was really needed. He had seen a case recently, who had been operated on by Mr. A. Gough, still alive 20 years after only a local excision.

Miss Kaye reported a similar case in which the tumour was the size of a grapefruit and situated on the right labium and partly on the left labium. She excised the tumour, and the inguinal glands at a second operation, and the section showed it to be of a low grade malignancy.

Dr. D. Fletcher Shaw said that Professor Morris had described a number of cases at a recent local staff meeting. These had all been given up as hopeless. He himself had seen one case thought previously to be hopeless. He did a local excision, and a dissection of the glands at a later operation, and the patient was still living 3 years later. She then developed a small plaque 2 inches from the skin incision—this was excised and there has been no further recurrence. How did these secondaries occur at some distance away in the skin, and why did simple excision cure them?

Dr. J. C. W. Somerville described a case of

CEREBRAL VASCULAR ACCIDENT IN LABOUR

The patient was a rather stout woman of 41 who had had 2 previous pregnancies in 1931 and 1937. The first was complicated by "inflammation of the kidneys and a twisted womb" but the second was uneventful.

She first attended the Antenatal Clinic at Dryburn Hospital on 17th October, 1951, when she was 16 weeks pregnant; her blood-pressure was 120/70 and the general condition satisfactory. Six weeks later she complained of slight bleeding, which was found to be caused by a 2.5 cm. long cervical polyp with a narrow base. This was twisted off easily without anaesthesia and was reported on as "a pedunculated glandular polyp. Histology shows a cervical polyp covered by squamous epithelium. At the base this appears rather hyperplastic but cell appearance is preserved in strands dipping into the stroma in which large cells are scattered—? decidual stromal change". Verbally, the pathologist expressed slight doubts as to the benign nature of the polyp, and slides were therefore submitted to Mr. Stanley Way and by him to Dr. Glucksmann, who reported that the growth was benign.

Apart from this, the patient's progress was satisfactory, until 35 weeks when her blood-pressure was found to have risen to 190/100. Her urine contained albumen ++ and she had oedema of her face, hands and feet. After admission to hospital the systolic pressure fell during the first week to 140, but rose again, remaining in the 160–170 region, the diastolic pressure being 100–110. After a medical induction had failed, 20 days after admission, the forewaters were punctured. Some 60 hours later labour commenced. The first stage was fairly rapid, Pethidine mg. 100 being given, and her blood-pressure rising to 180/110, but she felt well and had no signs of impending eclampsia. After some 3 hours in the first stage her respiration was noticed to be "grunting", and she said that she felt faint and thought she was going to die. Vaginally the cervix was found to be fully dilated. When she attempted to climb from the bed to the trolley—to be moved to the labour ward—she was unable to move her left arm and leg and complained that her face was twisted. She was then found to have a complete left hemiplegia. Her blood-pressure was 200/100, her mental state was clear and there was no neck stiffness, retraction or headache. The foetal head was visible and, before forceps could be applied, she had an easy face-to-pubes delivery of a 6 pound 13 ounces male child which had multiple abnormalities and died 7 hours after delivery.

One hour after delivery she felt well, her blood-pressure had fallen to 130/90, her face was less twisted and she could close her left eye. Her condition remained unchanged for some 10 hours, when she became comatose. Her eyes were turned up, her respirations were stertorous and her only reflex was withdrawal of the right leg when it was pinched.

Four hours later, (14 hours from the start of the

attack) she could be roused but was unable to concentrate. She was able to answer "yes" or "no" and complained of headache and pain in her chest. Tone, movement and deep reflexes were still absent on the left side. Her optic discs showed no abnormality. Lumbar puncture yielded clear fluid not under increased pressure.

At 18 hours she had a sudden onset of twitching of the whole of her face and right arm—the spasms being very violent. Between spasms the right arm appeared as flaccid as the left, but the right leg appeared normal. Paraldehyde 3 ml. intramuscularly controlled these spasms.

At 20 hours (2 hours later) she vomited, she was deeply comatose and her breathing was Cheyne-Stokes in character. Death appeared imminent, but during the night she improved and at 30 hours she could talk rationally and her right arm and leg power and tone had recovered. She still had a mild headache and her blood-pressure was 185/105.

During the following 3 days her mental confusion returned but her general condition improved and her facial muscles showed some recovery. Physiotherapy was commenced on her 7th postnatal day and on the 15th day she was transferred entirely to the care of the physicians. Their findings at this time were: right side—normal tone and reflexes, but on the left side the tone was increased; all arm jerks were brisk; knee and ankle clorus were present; and the Babinski response was present.

A course of Priscol, 2 ampoules daily, was started with very slight improvement and by the 26th day she showed only a flicker of movement in her left arm and leg. A stellate ganglion block was then performed with dramatic results. During the following 3 days she regained full movement of her limbs and within 2 weeks she could walk well with the aid of a stick. Unfortunately, the injection also affected her left vagus nerve, so that she lost her voice and had a marked sinking feeling in her abdomen. She refused a repetition of the injection.

When she was seen 2 months after discharge, she walked well with a stick, her left face showed slight residual weakness as did the flexors and extensors of her left elbow and knee, and the dorsiflexors of the left ankle. She also complained of slight dimness of vision of the left eye. Her blood-pressure was 140/90. Obstetrically, apart from some laxity of the vagina, she was well.

The points of interest in this case were, Dr. Somerville said, firstly the nature of the polyp. In some at least of these polyps occurring in pregnancy the clinical course was much less benign than one might hope, and this patient was being followed up with cervical smears.

Secondly, cerebro-vascular accidents in relation to pregnancy and labour were uncommon. The incidence reported by Stander was 1 in 33,000 and they were responsible according to Munro Kerr (1933) for 0.75 per cent of maternal deaths. Martin and Sheehan (1941) had pointed out that thrombosis of the cerebral veins in the puerperium has in the past been confused with eclampsia but records of such incidents occurring in labour were rare.

In the diagnosis of the present case the more common vascular accidents were considered and excluded, chiefly in view of the rapidly altering signs and symptoms and, in particular, the Jacksonian convulsions and transitory paresis of the contralateral arm which could not be explained in terms of space occupation by either haemorrhage or oedema at the site of the original lesion. Sub-arachnoid haemorrhage neither fitted the clinical picture nor the lumbar puncture findings. There was, however, a very striking similarity to the 2 cases described by McNairn (1948).

The first of these was also a gravida-3, who had had a toxaemic first pregnancy, and her attack was precipitated by lifting a heavy dustbin, pressing it against her abdomen as she did so. The other case a primigravida, had 3 episodes of a Jacksonian type before her final hemiplegic attack, and McNairn suggested that these were in fact cases where a small thrombus had become detached from the placental site and under the influence of straining had passed up the vertebral veins to the cerebral venous circulation. This mechanism was demonstrated in the cadaver and on monkeys by Batson (1940) and was postulated in this case. As McNairn stated, "In both these cases the slow onset of symptoms suggested a spreading venous thrombosis rather than a sudden haemorrhage or embolism".

REFERENCES

Batson, O. V. (1940): *Ann. Surg.*, **112**, 138.
Kerr, J. M. M. (1933): *Maternal mortality and morbidity.* Livingstone, Edinburgh.
McNairn, J. (1948): *J. Obstet. Gynaec. Brit. Emp.*, **55**, 630.
Martin, J. P. and Sheehan, H. L. (1941): *Brit. med. J.*, **1**, 349.

*Discussion*

The President had seen a similar case which recovered in 16 days. He thought the pathology must be localized brain oedema.

Dr. Somerville, replying to a questioner, said that angiospasm was a possibility but the physicians no longer considered it a fashionable cause.

Mr. D. C. Racker read a short paper on

THE MANAGEMENT OF POSTMATURITY

His main contention was that there was still no reliable method of diagnozing postmaturity with sufficient accuracy to determine treatment.

Until such time as a way was found to appraise the condition of the foetus *in utero*, he felt that it was better to use the expected date of confinement as the standard on which to base management.

In an attempt to establish whether or not it was safe for the foetus to be born at the expected date (E.D.C.) or near it rather than later, a series of cases were investigated at Park Hospital.

Patients attending at the antenatal clinic were divided into two groups simply by the day of attendance and with no obstetric selection. One group were allowed to continue until they started in labour naturally. In the second group, they were brought into hospital on the day before E.D.C. and on the E.D.C. were given simple stimulation such as hot baths, enemata, etc., but no drugs. If they had not started in labour by the day after the E.D.C. the membranes were artificially ruptured. There was no obstetric discrimination at all.

The reason for choosing the day after the expected date of confinement was because it was thought that it would be a means of finding if there was a large proportion of premature babies and also to have a basis for further investigations using varying periods after the E.D.C.

To have a standard of comparison in the same hospital and conditions, the foetal mortality in mature 'term' cases for the 18 months of the investigation were looked up. Term for this purpose was 7 days before to 7 days after the E.D.C.

The results were as follows:

| | | S.B. | Per cent. |
|---|---|---|---|
| Mature cases ... | 1229 | 19 | 1.54 |
| Induced cases ... | 205 | 3 | 1.46 |
| Postmature cases ... | 410 | 19 | 4.63 |

When the postmature cases were further analyzed it was found that 259 were from E.D.C. to +14 days with 6 S.B. = 2.31 per cent; 149 were more than 14 days past the E.D.C. with 13 S.B.s = 8.72 per cent.

Figures from the literature were given and also a survey of work on intra-uterine asphyxia, all of which bore out the author's contention that postmaturity was a very real danger.

*Discussion*

Mr. C. J. K. Hamilton said that, of the foetal deaths in his series of postmature cases, 50 per cent had no cause other than the postmaturity and most of them were intra-uterine. After term a degree of oligohydramnios developed. If this were marked the induction-delivery time might be unduly prolonged with bad effects for the child.

He believed that the ripeness of the cervix was a sign of maturity and that if it was not ripe the baby would come to no harm. If the cervix was ripe the membranes should be ruptured as soon as the patient reached term by dates.

Mr. G. W. Theobald remarked that the incidence of postmaturity varied geographically. It did not occur in the East, nor in Dublin, but was prevalent in Yorkshire. He had seen 3 cases of eclampsia at the 44th week. If induction killed no more babies than did postmaturity, then induction of labour was proper treatment.

In reply Mr. D. C. Racker said that the mortality from induction was less than that of postmaturity. In particular there were twice as many neonatal deaths in the postmature as in the induced cases. It would therefore be helpful to have some unanimously agreed method of dealing with postmaturity.

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

April 1953

A Meeting of the North of England Obstetrical and Gynaecological Society was held in the Jessop Hospital, Sheffield, on Friday, 17th April, 1953. The President, Mr. D. Currie, was in the Chair.

Mr. J. G. Napier described

### A Fatal Case of Staphylococcal Septicaemia Following Normal Delivery

Owing to the possibility of resistant strains of organisms developing, said Mr. Napier, there was general agreement that the use of antibiotics should be restricted to established infections of a major degree, and that sensitivity tests should be performed wherever possible. There was little place for prophylactic chemotherapy in obstetrics, and in gynaecology it should be limited largely to operations involving the lower bowel, or to proceedings such as a radical vulvectomy, in which sepsis was a special danger.

The purpose of the present paper was to suggest that conservatism in the use of these drugs can be carried too far, and that, in failing to give the most effective antibiotic at the earliest moment, the opportunity of curing certain types of infection might be missed.

*Case History*

The patient was a gravida-2, aged 39, who had had a previous normal delivery 9 years before. She had suffered from no significant medical illnesses, and the antenatal period was uneventful.

Ten days before the expected date of delivery, she was admitted to a Maternity Home in false labour. Three days later labour commenced spontaneously and within 24 hours a living female child was delivered, which weighed 8 pounds 4 ounces. The membranes had ruptured an hour and a quarter before delivery and the third stage of labour was normal. There was no record of any further vaginal examinations having been performed. Three days later her temperature had risen to 104°F and the pulse rate was 120. The abdomen was noted to be distended, and there was some suppression of the lochia. She was given Penicillin, 250,000 units 4-hourly, and Sulphatriad g. 1 4-hourly, and the following day Chloromycetin 750 mg. was given 6-hourly in addition. There was a definite response to this treatment, but when a high vaginal swab, taken at the onset of the illness, was cultured and grew a heavy growth of staphylococcus pyogenes, she was transferred 7 days after delivery

to the puerperal sepsis ward of the Jessop Hospital at Norton.

On admission the temperature was 100°F and the pulse rate 96. She was flushed, but in good general condition. Nothing abnormal was found in the heart and lungs but soft distension of the abdomen was noted. The fundus was felt 3 inches above the symphysis, and there was tenderness on palpation over the uterus and in the right iliac fossa. Bowel sounds were normal. Vaginally the cervix was lacerated and gaping. No adnexal inflammatory masses were detected. Large doses of Penicillin were given and other drugs were discontinued. Two days later, however, a marked relapse had occurred. The temperature rose to 105°F, the colour became sallow and a right basal pneumonia was present with distressed respiration. It was considered that a staphylococcal pneumonia was now present, and that the organism appeared to be Penicillin insensitive.

Aureomycin 500 mg. 4-hourly was now given in addition to the Penicillin. A blood culture, taken at the height of the fever, grew staphylococcus aureus, coagulase positive. It was found to be sensitive to Penicillin 500 units per ml., Chloromycetin 25 micrograms per ml. and Aureomycin 16 micrograms per ml. The white cell count was 13,500 per c.mm. with 88 per cent polymorphs, and the haemoglobin was 59 per cent.

There was a quick response to treatment at this stage, but, when the Aureomycin dosage was halved 8 days later, pyrexia returned with rigours and a toxic iritis developed. Increase of the Aureomycin again controlled the infection and the improvement was such that, following a second reduction in dosage, it was considered reasonable to cease all antibiotics 35 days after delivery. High vaginal swabs during this period had grown *Bacterium coli* on one occasion and bacillus proteus on another. An X-ray of the chest was reported on as follows: "The base of the left lung is dull, but the rest of the lung fields are clear. There is a small effusion in the left pleura". The infection did not remain quiescent for long. Three days later pyrexia had returned, and the following day the patient, who had been looking quite well, was again very ill indeed. The abdomen was once more distended and vomiting ensued. A faint generalized purpuric rash indicated the return of septicaemia, and this was confirmed on blood culture, staphylococcus aureus again being recovered. More refined sensivity tests were carried out, and were reported on as follows: Sensitive to 0.1 micrograms of Terramycin per ml., sensitive to 0.1 micrograms of Aureomycin per ml., sensitive to 6.25 micrograms of Chloromycetin per ml., and sensitive to 4 units of Penicillin per ml.

Terramycin was given as 500 mg. b.d., supplemented by further oral dosage. A 4-day course was given with some subjective improvement, but pyrexia persisted and for the first time a cardiac murmur was noted. It was considered that the condition was one of uncontrolled bacteraemia and, though no focal signs were detected, the question of an endocarditis was raised. A course of Streptomycin was given. This was later supplemented by Penicillin and, when the combination did not control the temperature, Aureomycin was substituted for Penicillin with immediate effect.

A pint of fresh whole blood was given intravenously, and when a further X-ray confirmed that the left pleural effusion was still present, this was aspirated, 14 ounces of blood-stained fluid being removed. This was shown in the laboratory to contain sufficient antibiotics to inhibit a culture of the standard strain of Oxford staphylococcus aureus, and further to inhibit the growth of a culture obtained from the patient's own blood stream.

Sixty-three days after delivery she had been afebrile for a week and looked quite well. She was complaining of some tinnitus and deafness as a result of the Streptomycin. Two days later all antibiotics were discontinued, but 3 days after this, quite suddenly, she became ill again. A loud murmur was now heard on auscultation, all over the chest and, despite Aureomycin intravenously as well as orally, she failed to rally and died 73 days after delivery.

The salient features on postmortem examination were as follows: There was a yellow necrotic area on the upper posterior wall of the uterus at the placental site, and the veins from this area had undergone a septic thrombophlebitis.

Petechial haemorrhages were generalized throughout the abdomen, and an abscess on the spleen had ruptured, causing a sub-phrenic abscess, which was limited by the left lobe of the liver. A further septic infarct was found in the spleen. The left kidney had a yellow wedge-shaped septic infarct, and the right a number of local embolic lesions below the capsule.

The left lung base was adherent to the diaphragm and a serofibrinous pleurisy was present on this side. The myocardium was pale, soft and friable. The endocardium appeared normal except for a series of proliferative friable vegetations on the proximal surface of the mitral valve, which was showing early ulceration with rupture of the chordae tendiniae. No other pyogenic focus was found.

This case, said Mr. Napier, illustrated the following points:

1. The availability of antibiotics might lull one into a sense of false security in puerperal sepsis.

2. This was particularly true in the case of staphylococcus pyogenes infection. Infection by this organism was relatively uncommon at present but its significance was greater than in the pre-antibiotic era, because it was normally less sensitive to antibiotics than the more common puerperal pathogen, streptococcus pyogenes, and, in addition, it pre-eminently possessed the power, unlike streptococcus pyogenes, of developing drug resistance.

3. The general behaviour of the patient and the actual sensitivity tests showed that, of the many antibiotics used, Aureomycin was the most effective in

controlling the infection. Indeed, the pleural exudate not only was sterile, but was, in fact, highly bacteriostatic to the infecting strain of staphylococcus pyogenes. The fatal outcome of the disease was doubtless due to the failure of access of the antibiotic to the foci of infection, and, in this connexion, it is well known that staphylococcus pyogenes in puerperal infection is peculiarly liable to give rise to septic thrombophlebitic lesions by virtue of its coagulase activity.

4. The progress of the disease in this case could be summarized as: placental site infection, pelvic thrombophlebitis, generalized dissemination, secondary infective lesions in spleen, heart, etc.

During the first week following the initial rise of temperature the patient was treated by a variety of antibiotics, after which time treatment was instituted with Aureomycin, the drug of choice as judged by antibiotic assay tests.

5. It was unknown whether the outcome would have been the same had Aureomycin treatment been given from the start, but, in view of the concealed type of lesion that staphylococcus pyogenes tended to produce, it did seem of paramount importance that a full antibiotic assay should be made immediately the infecting organism had been isolated. It is only by this means that the chances of deep septic thrombophlebitis could be minimized.

6. Enormous dosages of Aureomycin might be given without necessarily being followed by toxic manifestations. As a matter of interest, the drug bill in this case was £49 13*s.* 8*d.*

7. The need for an effective antiseptic and aseptic ritual was as great now as in the pre-antibiotic era.

*Discussion*

Mr. T. Fitzgerald mentioned that antibiotics could now be given continuously by the intravenous route, and wondered if this would have been helpful.

Dr. Payne discussed the use of antibiotics in combination and suggested that Penicillin and Aureomycin might be antagonistic.

The President wondered if there should not have been a resort to surgery, say a hysterectomy, in view of the failure of medical treatment, but

Mr. Napier felt that the infection had disseminated beyond the range of surgery at an early stage in the illness.

Professor A. H. Claye read a short paper on

THE EVOLUTION OF A GYNAECOLOGICAL HOSPITAL
(The Hospital for Women at Leeds, 1853–1953)

Among many important movements started during that period of new movements, the reign of Queen Victoria, said Prof. Claye, was the gradual separation of gynaecology from surgery and medicine and the founding of new special hospitals for the treatment of gynaecological patients. Among the earliest was The Hospital for Women and Children at Leeds.

The first exclusively gynaecological hospital in the world was the Hospital for Women, Soho Square, London, founded in 1842 by Dr. Protheroe Smith, who was at first the only surgeon. The Samaritan Hospital for Women followed in 1847, and the Chelsea Hospital for Women in 1871. In the provinces, Manchester St. Mary's was founded in 1790 as a lying-in hospital, but from some indeterminate date not long after its foundation after-effects of childbirth were also treated there. At Liverpool a dispensary for the treatment of uterine diseases was started in connection with the lying-in hospital in 1841, and a special ward was added in 1855 for diseases peculiar to women. The Jessop Hospital at Sheffield was opened in 1864.

Lawson Tait and Ross Jordan founded the Midland Hospital for Women at Birmingham in 1871, and this was entirely gynaecological from the start.

The Leeds Hospital for Women was founded in 1853, the chief instigator being J. Ingham Ikin, one of the original surgeons, who also acted as secretary for 31 years. Children were included in the title of the hospital and were treated for many years by the same medical men as were the women, but at the meeting for the inauguration of the Hospital the two main speakers, Dr. Hook, Vicar of Leeds and Mr. J. S. Shaw, Mayor of Leeds, confined their remarks to the gynaecological side of the work. Dr. Hook concluded his speech by stating "The hospital is designed to promote the cure or mitigation of a large class of complaints from which old and young, high and low, among the female portion of the population alike suffer, and that from no fault of their own. The object is not simply to lessen pain and give ease at the approach of death. However excellent and praiseworthy these objects may be, they are not contemplated by the Hospital for Women. It does not indeed exclude cases of the most perilous kind, provided there is a prospect of cure, or at least of some material amelioration. But it is intended chiefly to check diseases in the earlier stages, and, as far as human skill and foresight may do so, to obviate lingering illness and premature death. It is designed to give strength and activity to those who were either disabled from performing the duties of life, or else perform them with difficulty and pain."

The Mayor stated that there were in his opinion three conclusive reasons in favour of a distinct institution. First, the peculiar delicacy of the class of complaints requiring treatment. Secondly, the importance of their early treatment, for which a comparatively private institution was desirable. Thirdly, perfect repose of mind and body, which in a large or general hospital was not attainable, but might be afforded in an institution where the numbers were limited and the wards private. The benefits of the London Hospital and those elsewhere had been extensively diffused. He had much pleasure in moving that such a charity be established in Leeds, being the capital of the West Riding.

The Hospital was first situated at 28 East Parade,

It was opened on 1st June, 1853. It is nowhere stated how many beds there were, but in the first year 52 in-patients and 470 out-patients were treated. The average annual cost of a bed was "at least £30." In 1855, the house adjoining the Hospital was taken, and by 1859 it was felt strongly that further extension was needed. By 1st October, 1860, the purchase for £3,000 of Springfield Lodge on the present site was completed. After this "the small lodge and vacant ground in front of the property was purchased . . . in order to keep the frontage open and obviate the erection of any nuisance."

The new hospital was opened on 21st October, 1861, by the Earl of Carlisle and the Bishop of Ripon; the Mayor, Mr. James Kitson, and the Corporation graced the proceedings.

It appears, from the numbers of patients admitted and the average duration of their stay, that the capacity of this hospital must ultimately have been about a dozen beds.

For many years after the opening of the Hospital recommendations for treatment were made only by subscribers. Patients were required to be "duly qualified according to the rules, and unable to pay for medicines." One rule stated that the Hospital was "exclusively for the treatment of diseases peculiar to women and children, and that none but females of respectable character be admitted." Subscribers often failed to keep to the rules, and repeated reference is made to this at annual meetings! The surgeons too did not keep the rules strictly, though no censure of them is recorded.

In the annual report for 1866 the house committee reported "that a great difficulty they and the medical officers have to contend against is the procuring of good nurses, especially at short notice, and it appears to them that some institution or organization for training nurses is much required as in London, Liverpool, Dublin and other places." The problem of maintaining a suitable and sufficient nursing staff was always recurring until at the beginning of 1933 the present arrangement with the Leeds General Infirmary was made.

The Hospital was founded before the start of the Crimean War, a time when the status of the nursing profession was very low, and it was rare for respectable women to enter it. Charles Dickens mentions in his preface written in 1867 to *Martin Chuzzlewit* that Sairey Gamp and Betsey Prig were true, not exaggerated, pictures of the type of nurse in attendance on poor people 24 years earlier, when the book was first published.

It is not surprising, therefore, that the Committee of the Hospital had difficulties with most of the early matrons. They were not extravagantly paid, for the first was appointed at a salary of £20 a year, and the third was in 1864 given a rise from £21 to £25, "this to be final." At one time in the 'sixties Florence Nightingale herself was consulted about the appointment, but it appears that her nominee left after less than two months, dissatisfied with the situation and with the accommodation provided. A later holder of the post remained only a fortnight. In 1874 the annual report recorded about a new matron: "It is of great advantage to have a matron who has been accustomed to nurse and take charge of the sick and be present at operations."

When he joined the staff in 1929, said Prof. Claye, the nursing was carried out by probationers, who usually stayed 2 years, under a trained permanent staff. The post of probationer at the hospital was a blind-alley occupation, and suitable persons were not readily obtained. In 1932, as part of a larger scheme of co-ordination, agreement was reached with the General Infirmary that all their nurses should receive their training in gynaecological nursing at the Hospital for Women, and there had been no serious shortage of nurses since then.

How the patients were nursed in the earliest days history, perhaps fortunately, does not relate. In May, 1885, when a nurse was being appointed it was stated that "the duties of *both* nurses should be precisely the same, each taking an equal share in both day and night work." Later in the year the medical staff recommended the appointment of a night nurse, at £20 per annum plus uniform. Professor Charles Wright, speaking at the annual meeting in 1906, recalled that in 1886 "we had just two nurses, but neither of them had gone through their full training." At the time when he was speaking the number of nurses had risen to 14. Today with 103 beds in use the full strength of the nursing staff is 54, 32 probationers and 22 permanent staff.

In 1884 Mr. Ikin resigned. Rumour had it that Ikin, who may be called the founder of the hospital, founded it largely because he had been disappointed at not being elected to the Staff of the General Infirmary. Be that as it may, he threw himself wholeheartedly into establishing, extending, and improving the Hospital for Women and Children. So delighted with him were his fellow members of Committee that in 1863 "the Committee met at the President's (the Vicarage) by invitation to breakfast" and made him a presentation of a large quantity of suitably inscribed silver.

He combined the duties of surgeon with secretary, and the minutes of the Hospital meetings for the first 30 years are nearly all in his almost completely illegible handwriting. He resigned from the post of surgeon in May 1884, and at the December meeting of the Committee a letter was read from him announcing his intention to retire from the secretaryship at the next annual meeting. In January various general expenses of management in the Secretary's book were queried, and an explanation of them was demanded, Mr. Ikin not being present. At the next meeting the Committee resolved to allow the charges referred to at the previous meeting "as similar charges had been made in former years and not disallowed."

At the annual meeting in 1885 the Chairman regretted the absence of Mr. Ikin, who for 31 years had never missed a meeting. Mr. Ikin he said was

the originator of the Hospital for Women and Children. He had worked hard for its success and to him was largely due its present position. This was the only allusion to Ikin. His death in 1887 was only briefly mentioned at the annual meeting following it. Evidently something had occurred near the end of his connection with the Hospital to alter the previously happy relations between him and the rest of the Committee.

In 1885 the Committee, in discussing the re-arrangement necessary after the resignation of the secretary felt that any suggestion made by them must be regarded as merely temporary and provisional in view of the possibility of the amalgamation of the Hospital with the Infirmary. The secretary, Mr. Kirkby, was asked to write to the Infirmary Board saying that the Committee would be glad to appoint a sub-committee to confer with the Board or any of its members as to the future relations between the two hospitals. This was the first mention of this subject, and nothing came of it at the time; the two hospitals were ultimately brought under the same management by the Health Act in 1948.

Since 1872 there had been a special election Committee to make appointments to the honorary staff, and in October 1885 this Committee expressed the view that a woman should be elected as assistant surgeon. No objection to this was raised by the male members of the staff, but at the subsequent annual meeting after a discussion a resolution was passed "that it is not desirable to add to the medical staff at present."

Up to this time there had been no resident medical officer. The need for professional help additional to the honorary staff was now being felt, and in 1889 the appointment of an " anaesthetist and hospital assistant for three months " is mentioned.

Early in 1893 tenders were produced for a new out-patient department, and " a new and commodious out-patient hall " was opened on September 1st of that year.

In 1894 the first house surgeon took up residence, and in 1896 an anaesthetist was appointed in addition to the house surgeon.

At the annual meeting in 1897 the chairman, Mr. J. R. Spark, announced an anonymous gift of £4,000 to the Hospital. He thought it should be used for a building fund to start a new hospital, housing at least 100 patients and including a lying-in department. The donor agreed to this, provided that another £4,000 could be raised from other subscribers for the same purpose.

It was originally hoped to build a gynaecological wing of 50 beds at a cost of about £20,000 with a separate maternity department of 16 beds at a cost of £13,000. Unfortunately this proved to be too costly and in December 1898 it was resolved ' not to proceed with the proposed maternity department '.

In this year the Hospital received £8,000 under the will of Robert Arthington; this brought the building fund up to nearly £15,000 and justified a start on the new hospital. The clearing of the ground for the building was begun on 2nd September, 1901. They worked quickly in those days, so that in October 1902 the new out-patient department come into use, and the old wooden waiting room was pulled down. Presumably this old waiting-room was the " new and commodious out-patient hall " alluded to under the date 1893. At the suggestion of the honorary staff, a separate part of the building was equipped as a small lying-in department. On 30th October, 1903, Lady Mountgarret opened the new hospital. This ceremony coincided with the Jubilee celebrations, the Hospital having beeen founded in 1853.

The Maternity department of 5 beds came into use about the middle of 1904 and by the next January the wards were fully occupied.

In May 1905 the Faculty reported that there was need for more lying-in accommodation. They suggested taking for a term of years a private house or houses which should constitute a department of the existing hospital, with the idea that eventually a separate lying-in hospital should be built, that could train midwives. However, the idea did not materialize, for in the same year the Leeds Maternity Home was founded.

In 1906 Lord Allerton and Mr. Charles Lupton, the Chairman of the Infirmary Board, interviewed representatives of the Women and Children's Hospital and of the Leeds Maternity Hospital. They concluded the amalgamation of the two institutions was at the moment impracticable. The maternity work of the city they thought should be divided between them so that the Women and Children's Hospital concentrated on cases presenting medical abnormalities, while the Maternity Hospital admitted patients needing in-patient care on account of poverty or poor housing. The Women and Children's Hospital should not open a home similar to the Leeds Maternity Hospital, but both institutions should take part in the obstetric education of medical students and pupil midwives.

There was a third institution contributing to the maternity services at this time, the Leeds General Infirmary. They had provided a domiciliary service since before 1890, when Dr. Croft, later one of our surgeons, was resident there, and they occasionally admitted a difficult maternity case to one of their beds.

In 1907 the University, which had received its Charter in 1904, asked all three institutions to provide facilities for practical training in obstetrics, and a joint committee was set up to consider this problem. Ultimately obstetric training was concentrated in the Maternity Hospital.

In October 1904 the first woman resident clinical assistant had been appointed. This was Dr. Laura Veale, sister of Dr. Rawdon Veale, now Consulting Physician to the Leeds General Infirmary. The Faculty, in reporting the appointment to the Committee, apologized for having acted *ultra vires*. They stated their reasons, first that they found " a lady could be boarded and lodged both suitably and

conveniently," and secondly, that "it was felt most emphatically that the best interests of the Hospital would be served by the appointment of Miss Veale; for besides being the only qualified applicant she will be able to devote the whole of her time to the duties of the Hospital, which her all-round training and experience should render most valuable."

A year later, the question of appointing a woman house surgeon arose. A woman was the best candidate, but it was felt inexpedient to appoint her "as it would expose the Hospital to outside criticism."

In April 1907 two house surgeons were appointed for the first time instead of one house surgeon and one clinical assistant. One of these two was the first woman house surgeon, Miss Edith Jones. For many years now the majority of residents have been women. They have served the Hospital no less efficiently than the men. Mrs. Poyser's favourite remark may be recalled: "I'm not denyin' the women are foolish; God Almighty made 'em to match the men."

In April 1908 the Faculty suggested that the gynaecological departments of the General Infirmary and the Women and Children's Hospital should be combined in our Hospital, and later that the nursing arrangements should be put under the control of the Infirmary. The scheme for co-ordination fell through, and the two suggestions were not carried out till 1933. The Committee would not accept the condition that the qualifications essential for honorary staff appointments should be the same as those required at the Infirmary, but apparently this was not their only objection to the scheme.

In 1912, after prolonged consultation with the General Infirmary, the children's work was handed over to them. The Hospital now became almost entirely gynaecological, the maternity work having dwindled owing to the expansion of the Leeds Maternity Hospital. However, it was not until the Annual Meeting in 1929, on the proposal of Dr. Croft, that the name of the Hospital was changed to "The Hospital for Women at Leeds."

Towards the end of 1928 it was decided to institute pay beds, if legal opinion decided that this could be done without infringing the rules of the Hospital. It was found that there was no objection, and so the old maternity department on the top floor was converted into a 6-bedded private block. This was opened to patients at very moderate charges on 1st January, 1930, and proved a useful addition to the private accommodation in Leeds for gynaecological patients.

Early in 1932 the General Infirmary asked if the Hospital for Women would take over completely the gynaecological work of Leeds; the Medical Faculty reported favourably on the idea, and the Committee then replied that it was prepared to take on the extra work. Twelve extra beds were to be provided in each of the two large wards as a preliminary, and it was hoped to build a new wing when funds allowed. The gynaecological teaching for medical students was transferred from the Infirmary to the Hospital for Women on 1st January, 1933. The Honorary Staff of the Hospital became members of the Joint Faculty with the members of the Infirmary Staff.

The Leeds Voluntary Hospitals Council came into being towards the end of 1933. Its function was to advise on questions of joint general policy for the General Infirmary, Maternity Hospital, and Hospital for Women. It was composed of lay representatives of the three hospitals, and the Joint Faculty, made up of the honorary staffs of all the hospitals.

During 1934 the very large waiting list was causing the Committee much concern, and it was decided after consulting the architects to convert the basement of the Hospital which had been left open when the 1903 building programme was completed, to "allow for free circulation of air beneath the entire pavilion", into a new out-patient department, the old out-patient department being turned into three small wards containing 25 beds.

The work, which had so far been held up for lack of funds, was begun in March 1936. On the advice of the Faculty, a second operating theatre near the main one was built over the new wards; this was necessary because of the large increase in the number of operations performed in recent years.

In 1937 the Almoner's Department was equipped, and the Pathological Laboratory was modernized for a newly-appointed pathologist. In 1938 the work of the Hospital continued to increase, the record number of 2,397 patients being admitted, and the record number of 2,290 operations being performed. The total number of beds in the Hospital was now 95: 83 public and 12 private.

During 1940 an extension to the pathological department was built at the lower end of the drive, providing an up-to-date laboratory.

For three months from the invasion of France in June 1944 the Hospital was receiving convoys of wounded soldiers: 192 men in all passed through. The men were so shy about heading their letters to their wives "Hospital for Women" that an appropriate military alias for the Hospital had to be devised.

In 1947 the building of a minor operation theatre attached to the out-patient department was begun, and additional accommodation for the Almoner and the Records department was provided.

In the last year of the Hospital for Women as an independent voluntary Hospital the amount of work done was still increasing, 2,921 patients being admitted and 3,009 operations performed.

On 5th July, 1948, the Hospital ceased to be independent, and became a constituent member of the United Leeds Hospitals, linked with the other teaching Hospitals, the General Infirmary, the Maternity Hospital and the Dental Hospital, under the management of a Board with Sir George Martin as Chairman.

Voluntary bodies continued to give valuable help. In 1950 the Ladies Guild of the hospital provided cubicle curtains with their metal fitttings for all the

public wards. The Committee, owing to difficulties of supply, had before 5th July, 1948, been able to fit them only in the 5-bedded wards attached to the largest wards.

At least 16 gynaecologists have undergone part of their training in the hospital and 8 specialists in other fields broadened their outlook by doing some gynaecology before passing to their life's work.

There was no tabulated list of operations and their results before 1890. It was not proposed to give full lists, but to show briefly the progress of surgery in the Hospital by means of the incidence and mortality of two standard types of operation, repairs (excluding vaginal hysterectomies) and abdominal hysterectomies.

In 1890 there were but 7 laparotomies and 10 perineal repairs. None of these cases was fatal, there was no hysterectomy and no colporrhaphy, and all the laparotomies but one were for ovariotomy.

In 1891, the word colporrhaphy appears for the first time, but there was not more than 1 in any year until 1899, when there were 2. The first hysterectomy appears in 1891: it was performed for a cystic fibroid, and the patient died.

| | | *Mortality* | *Per cent* |
|---|---|---|---|
| 1891–1900 | | | |
| Repairs ... ... | 104 | 0 | 0 |
| Hysterectomies ... | 5 | 1 | 20 |
| 1901–1910 | | | |
| Repairs ... ... | 249 | 2 | 0.8 |
| Hysterectomies ... | 176 | 18 | 10.2 |
| 1911–1913 | | | |
| Repairs ... ... | 283 | 0 | 0 |
| Hysterectomies ... | 187 | 10 | 5.3 |

From 1914 the abdominal hysterectomies are subdivided into subtotal, total and Wertheim's operation.

| | | *Mortality* | *Per cent* |
|---|---|---|---|
| 1914–1920 | | | |
| Repairs ... ... | 520 | 5 | 1.0 |
| Hysterectomies | | | |
| Subtotal ... | 329 | 7 | 2.1 |
| Total ... | 81 | 7 | 8.6 |
| Wertheim's ... | 45 | 4 | 8.9 |
| 1921–1930 | | | |
| The figures for the year 1926 are omitted, as for some unknown reason the deaths are not recorded. | | | |
| Repairs ... ... | 1193 | 6 | 0.5 |
| Hysterectomies | | | |
| Subtotal ... | 329 | 7 | 2.1 |
| Total ... | 342 | 12 | 3.5 |
| Wertheim's ... | 91 | 11 | 12.1 |
| 1931–1940 | | | |
| Repairs ... ... | 3113 | 20 | 0.6 |
| Hysterectomies | | | |
| Subtotal ... | 656 | 20 | 3.0 |
| Total ... | 721 | 27 | 3.7 |
| Wertheim's ... | 53 | 8 | 15.0 |
| 1941–1950 | | | |
| Repairs ... ... | 3837 | 8 | 0.2 |
| Hysterectomies | | | |
| Subtotal ... | 938 | 6 | 0.6 |
| Total ... | 1789 | 23 | 1.3 |
| Wertheim's ... | 85 | 3 | 3.5 |
| 1951 | | | |
| Repairs ... ... | 336 | 1 | 0.3 |
| Hysterectomies | | | |
| Subtotal ... | 35 | 0 | 0 |
| Total ... | 317 | 1 | 0.3 |
| Wertheim's ... | 27 | 0 | 0 |

The work done had increased enormously over the years. The mortalities have gone down progressively, except that in the decade 1931–40 all the figures were worse than in the preceding decade; but there was no record of the deaths in 1926. The 1941–50 figures were easily the best yet in all the types of operation recorded. The 1951 table suggested that the previous best might well be beaten in the current decade. There was a steady trend in Leeds as elsewhere in favour of total rather than subtotal hysterectomy and Wertheim's operation was being more frequently done with much greater safety. The main factors influencing the improved results were the use of sulphonamides and antibiotics, safer anaesthesia, increased resort to blood transfusion, and the skill of individual operators.

In the hundred years that had passed since its foundation, Prof. Claye concluded, the aims of the Hospital had widened. Obviously the relief of suffering women was still a major aim, but "the benefits to patients in the Hospital do not comprise the whole of the services rendered to the community. A succession of house surgeons hold appointments which enable them at the same time as they take part in the work of the Institution to gain knowledge and experience which will be at the disposal of their patients afterwards. The same applies to the large number of nurses whose training is carried out here. The concentration of similar cases in a special hospital affords opportunities for intensive study, which should result in further improvements" (Annual Report, 1923). Since that year many students of the Leeds School of Medicine had learned their gynaecology in the Hospital and by their presence and critical outlook had provided stimulation for their teachers.

Five of the deceased members of the Staff of the Hospital held the office of President of the North of England Obstetrical and Gynaecological Society: James Braithwaite in 1891; J. B. Hellier in 1900 and 1911; E. O. Croft in 1907; C. Oldfield ni 1921; and W. Gough in 1926. B. L. Jeaffreson was President-Elect for 1953 but did not live to take office.

Mr. D. H. Lees read a short paper on

TRANSVERSE ABDOMINAL INCISIONS IN OBESE GYNAECOLOGICAL PATIENTS

The problem of the stout patient who required a gynaecological operation which must be done by the abdominal route, said Mr. Lees, was a difficult one. This type of patient had a thick abdominal wall and often a dependent apron of fat, and they were frequently chesty and hypertensive, while previous abdominal scars might render the prospect even more gloomy.

The disadvantages of the usual vertical incision were the great depth of the wound and the difficult access to the pelvis; the necessity for steep Trendelenburg position with this particularly unsuitable type of patient; the considerable post-operative wound discomfort; the interference with movement of the diaphragm during and after operation leading to chest complications; and the distinct tendency to wound haematoma or sepsis and even burst abdomen.

Some better incision had to be found. In the first place a transverse incision planned to fall in the natural skin fold and below the greatest depth of fat seemed obvious—the Pfannenstiel incision. This method however did not give good exposure since the muscles were separated vertically and altogether the access was less satisfactory than with a vertical incision.

At this stage various surgeons had advised him to divide all the layers in one plane down to the peritoneum. This did not appeal to him particularly but he had tried it and found that it gave an easy and good approach to the pelvis. Unfortunately one could not approximate the cut muscle satisfactorily and it seemed that there must be a tendency to herniation.

Thereafter he had started to detach the recti muscles from the pubes right at their origin and he believed this was the answer to the problem. This was the basic step in the operation described.

The advantages were good access to the pelvis; the main mass of abdominal fat was avoided; steep Trendelenburg position was unecessary; there was little post-operative discomfort; diaphragmatic excursion was not impeded either during or after operation; there was little post-operative chest trouble; and the wound healed strongly with no tendency to herniation.

Mr. Lees continued that he did not claim that the operation was completely original. He later found that Cherney (1941) had described a very similar type of procedure although with a different method of closure and without the additional aids to exposure and resuture he himself employed.

Before projecting a film of the procedure, Mr. Lees described the steps of the operation.

1. A moderate Trendelenburg position was used and the lumbar curve was accentuated by using an inflated and folded rubber ring.

2. A curvilinear incision was made from below one anterior superior iliac spine to the corresponding point on the other side—the incision running in the skin crease. The fat was held back by the left hand.

3. The rectus sheath was opened transversely and the inferior epigastric vessels were identified in the lateral angle of the wound, and divided if desired.

4. The lower flap of rectus sheath was dissected off—right down to the pubes, carrying the pyradmidalis muscles on its under surface.

5. The rectus muscle on each side was defined, raised on the left forefinger and detached from the pubes—cutting on to the actual periosteum.

6. The muscles were pulled up and held back by tissue forceps exposing the peritoneum. From now onwards the pull of the muscles and the retraction of the upper flap of the rectus sheath acted as natural retractors and no metal retractor was required.

7. The peritoneum was incised fairly high and laterally to avoid the bladder and then opened transversely.

8. In closure the peritoneum was first approximated.

9. Next the rubber bag was deflated to restore the lumbar curve and a quick-acting intravenous muscle relaxant was given to make reattachment of the recti easy.

10. The muscles were reattached to the pubes, uniting fascia to periosteum by a series of interrupted catgut sutures. A running stitch was used laterally to close any bulge between the lateral edge of the rectus and the inguinal ligament.

11. The rectus sheath was reconstituted.

12. The skin was closed. Clips were shown on the film but stitches were better—and not many of these. Cagtut was used throughout; in the presence of all this fat, unabsorbable sutures were not suitable as they were likely to cause sinuses.

REFERENCE

Cherney, L. S. (1941): *Surg. Gynec. Obstet.*, **72**, 92.

*Discussion*

The President said he was never unable to gain exposure by a vertical incision. He considered that the main value of the transverse incision was aesthetic, and felt that removal of the apron of fat would be of value in stout subjects. Mr. P. Malpas considered that the transverse incision was the incision of choice in gynaecology except in the presence of enormous tumours. He elevated the anterior rectus sheath widely and used the Pfannenstiel approach. Miss E. Mills wondered if harm ever resulted from the use of the rubber bag in maintaining posture, and Mr. C. H. Walsh enquired whether detachment of the recti might not follow this operation. Mr. Lees, in reply, did not favour the removal of the fat apron as this might be followed by considerable sepsis. With the help of a relaxant he had not encountered difficulty in sewing back the recti to their original position. He had been using the method for 3 years, and had been very happy about the results so far.

Mr. T. F. Redman gave a short paper on

THE MINOR DEGREE OF HYDROCEPHALUS AS AN OBSTETRICAL PROBLEM

(This article appears at page 888)

*Discussion*

Mr. C. H. Walsh referred to an article in the *British Encyclopaedia of Medical Practice* (1951), in which 70 cases of hydrocephalus occurring in Liverpool were considered under 3 groups—gross, moderate and slight. The problem cases were in the second group, and in these the almost inevitable presence of spina bifida might account for the closed sutures. He agreed regarding the great value of cephalometry. Prof. A. M. Claye pointed out that when a large amount of head could be felt abdominally and a large amount could also be felt in the pelvis the case was one of hydrocephalus. Prof. C. Scott Russell reminded the members that in certain cases pressure of the pelvic bones on the base of the skull might lead to opening of the sutures of the vault, and an erroneous diagnosis of hydrocephalus. Mr. P. Malpas considered that much harm might come if the younger generation became unduly hydrocephalus minded, and Mr. Hamilton agreed with this. A Caesarean section producing a hydrocephalic infant was a lesser evil than the perforation of the head of a normal child.

# BOOK REVIEWS

"A Modern Practice of Obstetrics." By D. M. STERN and C. W. F. BURNETT. Baillière, Tindall, and Cox, London, 1952. Pp. viii + 248, illustrations 140; price 35*s*.

As the Preface indicates, "this book sets out the practice of obstetrics at the West Middlesex Hospital, and is the result of experience gained from some 50,000 consecutive deliveries during the past sixteen years". Elsewhere the Preface states: "Where our experience has been at variance with commonly accepted practice we have not feared to break alway from tradition". This threat of heterodoxy need not, however, unnecessarily cause alarm to the reader for he will discover as he reads that the authors, whilst introducing some novel features, have succeeded in no small degree in producing a book of merit based in the main on well established practice. The arrangement and handling of the subjects are good, the style is direct and readable, and in the selection of material there is a commendable emphasis on well tried experience and a discarding of much outworn material that tends to pass from one textbook to another.

One of the novel features is seen in the obvious pains of the authors to invest their book with a literary flavour. They publish as their "frontispiece" a long extract from William Smellie's *Treatice on the Theory and Practice of Midwifery* on the requisite qualifications of accoucheurs, midwives and nurses who attend lying-in women. They provide a long Appendix on Etymology in which the first three items are: *Abdomen*. L. abdere, to hide. The cavity where the internal organs are hidden away; *Abortion*, L. ab., away; oriri, to be born. Failure to be born; *Acromion*. Gr. akron, tip; omos, shoulder.

An interesting novel feature are the chapter-headings from Shakespeare, with which they introduce each of their chapters. These introductory headings, whilst they are invariably apt, and whilst they are a credit to the literary research of the authors, cannot fail to give considerable amusement to the reader. Chapter III, on The Clinical Features of Normal Pregnancy, is introduced by "Oh! How this mother swells up", from *King Lear*. Chapter IV on the Management of normal Pregnancy has "Your ladyship were best to have some guard about you", from *Twelfth Night*. Chapter VI, on The Toxaemias of Pregnancy, has "My womb, my womb, my womb undoes me", from 2 *Henry IV*. Chapter XI on The First Stage of Labour, has "The mouth of the passage shall we fling wide ope" from *King John*; and Chapter XII, on The Second Stage of Labour, "We'll put the matter to the present push" from *Hamlet*!

Here and there in the text we found ourselves in disagreement with the authors. In the few lines which they devote to the important subject of the softening of the pelvic joints during pregnancy, they make the statement: "The softening is in reality a form of preparation for the *excessive* movements of the pelvic joints which occur during labour" (the italics are ours). In the section on Accidental Haemorrhage reference is made to the risk of symmetrical cortical necrosis of the kidney, but no reference to the commoner kidney lesion. And there is no mention of the life-saving recent work, especially that of Bull, on the management of the anuric state.

The book is illustrated by line drawings, which are adequate for most purposes. But they fail occasionally to represent the object in a convincing manner; this applies especially to histological material.

"Physiological Bases of Gynecology and Obstetrics." By S. R. M. REYNOLDS. Charles C. Thomas, Illinois, U.S.A., and Blackwell Scientific Publications, Ltd., Oxford, England, 1952. Pp. xii+153; price 40*s*.

THIS is one of the monographs in the American Lecture Series edited by E. C. Hamblen. The lectures in this volume were delivered at the Facultad de Medicina de Montevideo. The Preface states that they are "intended for busy gynecotokologists who lack the time to make a detailed study of the large literature on the subject."

Much of the matter described in this book deals with the investigations of Dr. Reynolds himself and his colleagues at the Carnegie Institution of Washington. The approach is experimental rather than clinical; it is concerned with the fundamental physiological background to the clinical problem. Much of the work has been carried out since the appearance of the second edition of the author's well-known *Physiology of the Uterus* in 1949.

To many readers the freshness and novelty of the material and its presentation will create surprise and even excitement. In the description of the remarkable investigations of Dr. A. Csapó, for example, it is shown that the contractile system of the uterine muscle is a complex of two proteins, actin and myosin, which together, but not apart, are contractile. Uterine actomysin differs from striated muscle actomysin in having a longer latent period and in contracting more slowly and to a lesser degree. Following an irradiation menopause uterine actomysin is almost devoid of contractile power, that from the non-gravid uterus

shows appreciably more contractility and a more rapid rate of contraction, whilst at term it contracts rapidly. These actions are dependent upon the presence of adenosine triphosphate and the enzyme adenosine triphosphatase and both actomysin and adenosine triphosphate are dependent upon oestrogen for their proper action.

The book reviews and expands the previously reported and important work of the author and his colleagues on the patterns of uterine activity during dilatation, on uterine growth during pregnancy and on the physiological effects of uterine distension. In the chapter on The Physiological Basis of Menstruation the author points out how the concepts of only five years ago are being challenged. The absence of a system of coiled arterioles in the endometrium of the New World monkeys suggests that the basic mechanisms of menstruation are not dependent upon such a system.

This is an important book. It is a pity that for its odd 153 pages without illustrations we have to pay forty shillings.

"The Normal Child: Some Problems of the First Three Years and Their Treatment." By RONALD S. ILLINGWORTH, M.D., F.R.C.P., D.P.H., D.C.H. J. and A. Churchill Ltd., London, 1953. Pp. 342; price 30s.

"THE normal child", this is a bold title and it is a considerable feat to have written this book, covering as it does almost all aspects of children's development, behaviour and misfortunes in the first three years of life. The book is divided into four sections, feeding problems, physical problems, developmental problems and behaviour problems. That is Professor Illingworth's answer to the question "What is the normal child?"—a problem or perhaps a succession of problems. And indeed it is the best answer, for all, or nearly all, infant behaviour is determined by the encounter of his instincts and inner drives with outer circumstances, be they ordinary or extra-ordinary. When they are extra-ordinary we get problems.

He has collected and sifted a wealth of solid fact about the normal response to life of infants and small children. Beside these solid facts we have the many obvious faults of parents and the mistakes that they make. Many of these are due to temperament, which cannot easily be remedied, but most to ignorance which can. Over-protection, over-domination, rigidity of training, rejection, etc., and, in the child, a sense of insecurity, go a long way to explain many freaks of behaviour of the normal child. These are useful concepts and with them it is possible to help parents and sometimes to solve problems. Head-banging, alas, we see, is not one of these.

The book is written expressly for doctors and though it is also suitable for any educated lay parent there is no "writing down" to capture a wider public, which a book with such an appealing title might well do. Every statement of his own opinion is carefully weighed and clearly stated after quoting the best authorities. Sometimes, of course, these opinions cancel out and one is left no further on. The references, which represent only a selection of Professor Illingworth's reading round this subject, are all given at the end of the book. They number three hundred and thirty-five.

Many psycho-analytical opinions are quoted, without, of course, their wider context. The precepts on which psycho-analysts base their opinions are on the whole poorly understood and little accepted by paediatricians and doctors in the main. The effect of such quotations side by side with statements which, though less penetrating, are eminently sensible is sometimes ironical. This is probably not intentional as the author's attitude to these difficult questions is openminded and modest.

For instance, in discussing the basic causes of sphincter troubles (the normal development, rigid training, fissure in ano, attention-getting, etc., etc.) he states: "Whatever the cause of the reaction most would agree that unhappiness is a common cause of sphincter disturbances." Then follows Freud's explanation of deliberate withholding of stools. "Children utilizing the erogenous sensitiveness of the anal zone can be recognized by their holding back of faecal masses until through accumulation there result violent muscular contractions." And again: "The retention of faecal masses, which is at first intentional in order to utilize them as it were for masturbatic excitation of the anal zone, is at least one of the roots of constipation so frequent in neuropaths." The author then reiterates that he feels these problems to be due simply to the developmental trends and parental attitudes, of which he has given a description. This explanation is the only workable one for most of those who work in the field of child medicine.

There is an excellent section on Development, a subject on which Professor Illingworth is the chief authority in this country, and that most fascinating question of all, the prediction of intelligence and personality, is well discussed. There is a series of line drawings of the development of locomotion by Mr. A. Foster, Medical Artist to the United Sheffield Hospital. Some of the children are charmless, awkward and, annoyingly, of indeterminate sex; but they do show exactly what it is required to illustrate. Though based largely on Gesell, this account of development escapes almost completely from the ingenious but irksome vocabulary of that author. Must we, however, endure "vocalizations"?

The section dealing with infant feeding and the newborn infant's very special problems is one of the best. Self-demand breast-feeding is extolled, and its advantages well argued. There is a terrifying and salutary chapter on the dangers of cross-infection in infants' nurseries and the means of diminishing them.

The book is ably compiled and easy for reference. The style is plain. It will certainly be of lasting value to paediatricians and all who have responsibility for the health of children. *Dermod MacCarthy*

"Brain Surgeon." The Autobiography of William Sharpe, with a foreword by Sir Cecil Wakeley, Bt., P.R.C.S. Victor Gollancz, Ltd., London, 1953. Pp. 244; price 16s.

This is the story of a pioneer of neurosurgery whose earliest memories are of austere and rigidly orthodox Presbyterian family life in a mission to a slum area of a great American city. Escaping from his Calvinist father's desire for his son to enter the ministry, Sharpe followed the example of seven uncles and two brothers by studying medicine. His entry to Harvard was helped by athletic prowess but soon he earned his own way, making enormous sums of money by tutoring fellow students and thus affording a year in Europe. He gives an interesting account of the great figures in Berlin at the beginning of this century and a lively description of the comforts and relaxations as well as the strife of life in a German student corps. Returning to the United States to complete his medical training, he saw something of the Golden Age at Johns Hopkins, being attracted particularly by Cushing. After two years of general surgical experience in New York he returned to Johns Hopkins in 1911 for a year in neurosurgery. The description of Harvey W. Cushing is a feature of the book. The following year was spent as surgeon to the newly formed Harvard Medical School of China in Shanghai. A correct diagnosis and appropriate operation for haemorrhage compressing the brain of the son of the President of China won him high prestige and rich reward. In 1913 Sharpe returned to New York and commenced his life career in neuro-surgery. The remainder of the story, written with a pleasing fluency, is more than a professional success story and has interest beyond the neurological surgical background to appeal to all medical readers. Those readers with a special interest in the care of the newly born will follow with attention the result of spinal puncture by this expert neurosurgeon of a consecutive series of 500 newly born babies in the search for signs of unsuspected intracranial damage as judged by elevation of the spinal pressure and the presence of blood.

Sharpe is confident that cerebral palsy in an infant is in most cases the result of detectable intracranial damage at birth and he evidently believes that other less striking nervous disorders may follow less severe haemorrhages. His case is that by suspecting the twitching or lethargic newly born baby, spinal puncture may reveal signs of raised intracranial pressure and haemorrhage: repeated spinal punctures will drain away blood which might otherwise coagulate and form an organization residue along the supracortical veins, permanently impeding absorption of cerebro-spinal fluid. He cites examples from his own practice where operations to relieve abnormal intracranial fluid tension have restored normal function and behaviour. Towards the end of his book he reveals that his purpose in writing his autobiography is to emphasize his conviction that cerebral palsy may be prevented in over 70 per cent of cases by avoidance of birth trauma and early diagnostic puncture in suspected babies. He states that there are 300,000 cerebral spastic children in the United States.

Reference to the author's publications includes two books on neurosurgical subjects and 65 articles in medical journals. A defect of a bibliography of 34 references to books and papers confirming intracranial birth haemorrhage as a cause of cerebral spastic paralysis is the absence of any reference later than the year 1924. *Duncan Murdoch*

"Clinical Obstetrics." By C. B. Lull and Robert A. Kimbrough. J. B. Lippincott Company, London, 1953. Pp. 732, illustrations 392, 8 colour plates; price 80s.

The editor of this book and its contributors have reason to be proud of this new book on Obstetrics, which has been published in timely fashion when the Pennsylvania Hospital is just 200 years old, and it is sad that Dr. Lull's death has prevented his seeing the fruition of his work as the original editor.

The book is arranged in sections dealing with every aspect of obstetrics, and the foreword contains an interesting historical review of the development of its parent hospital.

It is inevitable with so many contributors that the mode of presentation should vary, so that the impression gained is somewhat uneven. Much of the material is excellent. Dr. Bishop's chapter on Obstetric Radiology is particularly outstanding, and that on Anatomy by Dr. Muckle and Dr. Kern deserves special mention for its clarity and its emphasis on the obstetrical viewpoint. Dr. Tompkins's chapter on Nutrition and Nutritional Deficiencies is of the greatest interest.

In the preface, the editor states that the book "is a record of practice, rather than an encyclopedia of obstetrics" and that the material included is chiefly that "which the student and the practitioner require for rational care of the pregnant patient". It is surprising, therefore, that the management of placenta praevia is not described in more detail, the avoidance of vaginal examination and the role of blood transfusion not even being mentioned. Again, in the section on diabetes and pregnancy, the dangers of ketosis and pre-eclampsia are not mentioned, nor is the mode and time of delivery discussed, while under *abruptio placentae* the possibility of anuria does not achieve recognition. It is surprising, too, that no reference is made to the place of valvulotomy in mitral stenosis complicating pregnancy. It is gratifying, however, to note that in discussing routine antenatal examination a systolic blood-pressure of 130 mm. Hg is regarded as suggestive of hypertension—a figure which requires wider acceptance.

The production of the book is excellent, and the illustrations are lavish and well chosen; the index is comprehensive.

As a "record of practice" this book is good, and

is worthy of close acquaintance, providing as it does a window on contemporary practice by the staff of one of the well-known hospitals in the United States. But the student and general practitioner will require to supplement his knowledge by recourse to one of the standard text-books to fill, however briefly, the many gaps which are here apparent.

"Gynecological and Obstetrical Pathology." By PETER A. HERBERT, M.D. Henry Kimpton, London, 1953. Pp. 683, illustrations 428, including 2 coloured plates; price 93*s.* 6*d.*

THIS is a strange book. The author is Professor of Pathology at the Jefferson Medical College, Philadelphia, and, as we should expect from a writer of this standing, the sections which deal with the author's own speciality are in general satisfactory. The descriptions are clear, the illustrations are numerous and of a high order, and the literature under each chapter is comprehensive. But even in these sections the banal will every now and then break through. Thus, in the discussion of the "Cause" of Carcinoma of the Cervix under 10 headings, the 7th heading is: "*Viruses.* Although viruses as a cause of cervical cancer have been incriminated, direct proof of their role is lacking. A derangement of intracellular enzymes in the production of cervical carcinoma cannot be denied, but the exact alterations which take place are not known."

Under Rupture of the Uterus it is stated that the incidence "as recorded in the literature varies from one in ninety-five to one in 3,029 deliveries. The ages of the patients usually [*sic*] vary between fourteen and forty-eight years." The causes of rupture of the uterus are reviewed under 14 headings as follows: (1) *Gravidity,* (2) *Uterine cicatrices,* (3) *Malposition of the uterus,* (4) *Cervical stenosis,* (5) *Congenital anomalies,* (6) *Prolonged labour,* (7) *Invasion by hydatid mole,* (8) *Tumours of the uterus,* (9) *Overdistension* ("polyhydramnios has been recorded to cause spontaneous rupture in three cases. In a fourth case, pituitary extract was also given."), (10) *Placenta,* (11) *Foetus,* (12) *Pelvic abnormalities,* (13) *Vagina* and (14) *External causes.* It is strange to find no apparent appreciation of the close relation between foetal and pelvic abnormalities and prolonged labour.

In the section dealing with tuberculous salpingitis there is the statement: "Its frequency, as compared with other types of inflammations of the fallopian tubes, has been recorded as varying from 2.7 to 11.5 per cent (Greenberg)." It is not clear what the basis of comparison is. Again under tuberculous salpingitis there is the statement: "*Local symptoms* due to infection itself and to its effect upon the endometrium consist of pain in the lower part of the abdomen, dysmenorrhea, amenorrhea, scanty or irregular menstruation, and sterility".

The volume is well produced in regard to type, paper and binding.

"Diseases of Women." By Ten Teachers. Under the Direction of Frederick W. Roques. Edited by F. W. Roques, J. Beattie and J. Wrigley. Ninth Edition. Edward Arnold and Co., London, 1953. Pp. 480, illustrations, 179; price 28*s.*

IN this edition Mr. Clifford White, Sir William Gilliatt and Mr. Frank Cook have been succeeded as co-editors by Mr. Stanley Clayton, Mr. Calvert Gwillim and Mr. Thomas Lewis. The Preface states that, in this edition, the editors have aimed at "an increase in dogmatism, in which the book has previously been said to be deficient, without sacrificing orthodoxy." The chapters devoted to the endocrine glands, the hormones and the physiology of the menstrual function have been completely rewritten, whilst those on infections, including venereal diseases, have been largely rewritten. Fifty-three new illustrations have been added.

This edition maintains the high standard achieved by previous editions. By the adoption of a simple and direct narrative style, by careful selection and by a wise choice of emphasis, the authors have succeeded admirably in their declared object of producing a textbook "written primarily for young practitioners and medical students."

The only section of the book which we find to be unsatisfactory is Chapter XLII on "Neurasthenia and Neurosis in Relation to Pelvic Disorders". We fear that to the young reader this chapter, on an admittedly difficult subject, will bring little enlightenment.

The editors and publishers are to be congratulated on the general appearance of the book and on the paper, type, binding and illustrations. The only illustration that falls below the general high standard, which has obviously been aimed at, is Fig. 27, "Erosion of the Cervix", which is poor.

"Advice to the Expectant Mother on the Care of Her Health and that of Her Child." By F. J. BROWNE, M.D., D.Sc., F.R.C.S.E., F.R.C.O.G. Tenth edition. E. and S. Livingstone, Ltd., Edinburgh and London, 1953. Pp. 48; price 1*s.*

THIS booklet, first published in 1926, has been revised for the tenth edition. The sections on Body Clothing and the Care of the Premature Infant have been contributed by Sister Edwards, University College Hospital, London. The elaboration of the maternity services during the intervening 27 years has not diminished the need of the newly expectant mother for reliable, clear and simply written information which she can read, perhaps with her husband, at home. This new addition meets the need admirably and will be found commendable alike by private obstetrician and clinic authority.

The author emphasizes the importance of noting carefully the date of the last period. In a future edition

it might be an advantage to ask also for a careful note to be made of the time when foetal movements are first felt as a useful check on the progress of pregnancy.

"Gynäkologische Organneurosen." By PROFESSOR DR. HANS ROEMER. Georg Thieme Verlag, Stuttgart, 1953. Pp. 190; price DM.13.50.

THIS book is intended for students, general practitioners and gynaecologists, and deals with the psychosomatic and psychotherapeutic problems of gynaecology. In the opinion of the author 10 to 20 per cent of all patients complaining of gynaecological disturbances are not suffering from organic disease, and he feels that there is an essential need for instruction of "the ordinary doctor" in the recognition and treatment of psychosomatic conditions.

Professor Roemer tackles this task by introducing his readers to modern psycho-analytical techniques, and praise is due to him for doing this in clear, simple language, avoiding complicated technical terms wherever possible and interspersing his theoretical digressions with many practical illustrations of behaviour.

The subject is discussed from various angles, e.g., pathogenesis, symptomatology, disposition to neurosis, constitutional factors, diagnosis with special reference to interpretation of dreams and associations, and therapy. The second part of the book is taken up by case histories.

Although Professor Roemer states his case well and sounds convincing, it seems a tall order to ask gynaecologists to qualify as psychotherapists. It is doubtful whether, after reading through this small volume, excellent though it is, the gynaecologist will have gathered enough enthusiasm to devote years of study to psycho-analytical technique and, if he does, one shudders to think of what will become of his gynaecology.

# REVIEW OF CURRENT LITERATURE

## CONTENTS


| | REF. |
|---|---|
| ANATOMY | 236 |
| PREGNANCY | 237 |
| LABOUR | 257 |
| PUERPERIUM | 261 |
| ANAESTHESIA | 262 |
| INFANT | 264 |
| GYNAECOLOGY | 268 |
| Sterility | 273 |
| New growths of the reproductive organs | 281 |
| Operations | 287 |
| Urology | 289 |


## ANATOMY

236. **Histologic Study of the Pelvic Connective Tissue.**

By B. BERGLAS and I C. RUBIN, *Surg. Gynec. Obstet.*, **97**, 277–289, Sept. 1953. 13 figs. 19 refs.

For the microscopic examination of the pelvic connective tissue the authors used two adult pelves. The first was the entire pelvis of a 23-year-old nullipara removed from the body 3 days postmortem. The pelvic arteries and veins were injected with latex via the aorta and inferior vena cava. The pelvis was then fixed in 2 per cent formaldehyde, decalcified in 5 per cent hydrochloric acid solution and bisected in the sagittal plane. The two halves were frozen and one was cut into sagittal sections and the other into coronal sections 1–1½ cm. thick. These were subjected to the usual histological processes and stained with haematoxylin and eosin, Mallory, van Gieson and Verhoeff stains.

The second pelvis was treated in the same way except that injection of the vessels was unnecessary as they were found to be completely filled with coagulated blood.

On microscopic examination of the sections the authors find that the subperitoneal space of the pelvis is filled with loose areolar connective tissue, which is continuous with the retroperitoneal connective tissue of the abdominal cavity. The so-called cardinal ligament and pubovesico-uterine ligament do not exist. Instead blood vessels are found embedded in loose areolar connective tissue and nowhere in these areas can any dense fibrous tissue be found with fibres grouped into large bundles as seen in ligamentous structures.

The unstriated muscle fibres, not infrequently referred to as present in the parametrium, can be traced in the sections as originating from the vessel walls. In the parametrial connective tissue layer there are also sparse elastic fibres which, however, do not exceed the amount found in the retroperitoneal connective tissue of the abdominal wall.

Anatomic analysis of the structures at the lateral pelvic wall shows that the connective tissue component of the parametrium is only in loose contact with the pelvic fascia. There is no fixation of the parametrium to the pelvic wall through the medium of a connective tissue attachment to the pelvic fascia. The commonly assumed fixation of the parametrium to the pelvic wall can be explained by the fact that the arteries and venous plexuses, embedded in the areolar connective tissue of the parametrium, are continuous with the main venous and arterial vessels situated at the pelvic wall.

The authors conclude that there is no anatomic basis for ascribing support of the pelvic organs to connective tissue structures. *John P. Erskine*

## PREGNANCY

237. **The Cytology of Normal Pregnancy.** (Die Cytologie der normalen Schwangerschaft.)

By A. KOLLER and J. ARTNER. *Gynaecologia (Basle)*, **136**, 137–151, Sept. 1953. 8 figs. (including 2 colour plates). 16 refs.

This study is based on vaginal smears examined at 4-weekly intervals in 725 normal pregnant women. Smears were examined after staining by the methods of Papanicolaou, Best and Gram. In addition studies were made of vaginal pH and in some of the cases estimations of hormone excretion were studied in addition. An attempt is made to correlate hormone excretion with the type of cell encountered in the vagina. In pregnancy four main types are encountered described by the authors as "navicular", "precornified", "cornified", and "cytolytic".

The authors do not regard the vaginal smear as necessarily diagnostic in pregnancy since the cells described may be found in non-pregnant women.

*Josephine Barnes*

238. **Studies on the Vascularization of the Human Placenta.**

By F. BOE. *Acta obstet. gynec., scand.*, **32**, Suppl. 5, 1953, 92 pp. 49 figs. 26 refs.

This beautifully illustrated monograph of 92 pages comes from the Research Department of Nyegaard & Co., Oslo. It is in 2 parts, "Foetal Circulation" and "Maternal Circulation". The results of the author's research are too numerous and too detailed to lend themselves to comprehensive abstracting, but here are the salient points. The peculiarities of the pattern of both the foetal and the maternal vessels appear to be designed to reduce the rate of blood-flow; this reduction is necessary to enable the interchange of materials between the foetal and the maternal circulation to be carried out satisfactorily. The vascular peculiarities on the foetal side are: Increase in diameter of the umbilical arteries when entering the chorionic plate, early division of the arteries inside the stems, elongated course of the branches of the stem-arteries, smaller diameter of the supply-arteries as compared with that of the sinusoid expansions of the villous capillaries. On the maternal side, reduction in the rate of blood-flow appears to be produced by the spiral arteries running for some distance in the basal plate before emptying into the intervillous space. The arteries enter the centre of each cotyledon. From the intervillous space the maternal blood leaves each cotyledon through numerous venous openings situated at the margin of each individual cotyledon that is in or near the placental septa.

The direct connections between the foetal paravascular capillary network and the venous system (i.e., the arterio-venous communications) are assumed to form the anatomical basis of a shunt mechanism.

*N. Alders*

239. **Measurement of Uterine Blood Flow and Uterine Metabolism. II. The Techniques of Catheterization and Cannulation of the Uterine Veins and Sampling of Arterial and Venous Blood in Pregnant Women.**

By N. S. ASSALI, R. A. DOUGLASS, W. W. BAIRD, D. B. NICHOLSON, and R. SUYEMOTO. *Amer. J. Obstet. Gynec.*, **66**, 11–17, July, 1953. 3 figs. 3 refs.

In this paper the authors describe the techniques of catheterization and cannulation of the uterine veins and sampling of arterial and venous blood in pregnant women with the object of measuring uterine blood-flow. Two techniques are described. In the first, the uterine vein is catheterized by an extra long Cournand catheter passed under fluoroscopic examination successively from the basilic vein to axillary and right innominate veins, superior vena cava, right atrium, inferior vena cava, hypogastric and uterine vein. In the second method the uterine vein is cannulated during Caesarean section or abdominal operations. Arterial blood is got directly from the brachial or radial artery. The uterine blood-flow is determined by the nitrous oxide technique and application of the Fick principle as used to determine cerebral blood-flow. No results are given in the present paper.

The method involves certain difficulties and hazards. Cardiac arrhythmia occurs very frequently during passage of the catheter through the right atrium. The amount of radiation to which the patient and foetus are exposed must be limited as much as possible but actually 2 or 3 exposures of 5–10 seconds' duration are necessary until the catheter reaches the heart, and, of course, much longer before the uterine vein is entered. Another risk is pulmonary embolism but the main drawback is failure to enter the uterine vein—the failures far outnumber the successes. A serious objection to the cannulation technique is that the number of venous blood samples that can be got is limited as the abdominal cavity cannot be left open for more than 20 to 25 minutes without serious risk to the patient. Complete nitrous oxide equilibrium may not be accomplished within this period of time.

*F. J. Browne*

240. **Measurement of Uterine Blood Flow and Uterine Metabolism. IV. Results in Normal Pregnancy.**

By N. S. ASSALI, R. A. DOUGLASS, W. W. BAIRD, D. B. NICHOLSON, and R SUYEMOTO. *Amer. J. Obstet. Gynec.*, **66**, 248–253, Aug. 1953. 1 fig. 6 refs.

In previous papers the authors described techniques for obtaining samples of blood from the uterine veins by catheterization and cannulation, and discussed the possible application of the nitrous oxide method to the measurement of uterine blood-flow in non-pregnant and pregnant women. The present paper deals with results of specific measurements obtained in 48 normal pregnant or post-partum patients—30 of the former and 18 of the latter.

The blood-flow to the uterus during the last month of normal gestation varied from 12.2 to 18.5 ml. per 100 g. per minute with an average of 15 ml. per 100

g. per minute. Twenty-four to 48 hours after delivery the blood-flow to the uterus decreased to an average of 9 ml. per 100 g. per minute. The oxygen consumption of the pregnant uterus during the last month of pregnancy varied from 1.4 to 2.4 with an average of 1.9 ml. per 100 g. per minute. The resistance to the blood-flow in the uterine vascular bed varied from 4.5 to 7 mm.Hg/ml. per 100 g. per minute. In the post-partum period it rose to approximately 9. The rise was caused by a decrease in the blood-flow rather than by an increase in the mean arterial pressure. It is noted that the average value, 15 ml. per 100 g. per minute, is very similar to that obtained by Barcroft in pregnant rabbits. *F. J. Browne*

241. **Lactosuria and Glycosuria in Pregnancy and the Puerperium.**

By F. V. FLYNN, C. HARPER, and P. DE MAYO. *Lancet*, **2**, 698–704, Oct. 3, 1953. 3 figs. 33 refs.

The authors investigate the urine of the pregnant woman for sugar by the qualitative Benedict test and by paper partition chromatography. Urine specimens from 245 pregnant women, 372 unselected patients, 240 non-pregnant females and 132 males were investigated. They found that lactosuria was present in 50 per cent of the antenatal patient attendances as compared with 9 per cent of the controls (both male and female). The frequency of lactosuria was double that of glycosuria. The incidence of lactosuria increases steadily from the third month until the 34th–35th week of pregnancy when it remains stationary. Lactosuria was most common after delivery, 99 per cent of the patients having detectable quantities 4 days after delivery. The incidence of glycosuria rises sharply after the third month and fluctuates between 20 and 31 per cent for the remainder of the pregnancy. Immediately after delivery the glycosuria abruptly disappears. From the investigations carried out it appeared that lactosuria and glycosuria occurred as intermittent phenomena.

They conclude that the incidence of excretion of both sugars is lower in the multiparous patient than in the primigravida and that the incidence of lactosuria diminishes with increasing numbers of successful pregnancies. Age apparently had no effect on the incidence of lactosuria but the frequency of glycosuria probably increased with age. No association between the milder varieties of toxaemia and sugar excretion was detected in pregnancy. They suggest that glycosuria of pregnancy is due chiefly to a lowering of the renal threshold for glucose and that the lactosuria is chiefly mammary in origin. *H. H. Fouracre Barns*

242. **The Blood Volume in Pregnancy as determined by $P^{32}$ Labelled Red Blood Cells.**

By N. I. BERLIN, C. GOETSCH, G. M. HYDE, and R. J. PARSONS. *Surg., Gynec. Obstet.*, **97**, 173–176, Aug. 1953. 4 figs. 11 refs.

This paper is a report of studies of the blood-volume during the course of pregnancy as determined with $P^{32}$ labelled red blood-cells in 181 women.

The blood-volume was determined by a modification of the method of Hevesy and Serahn. Only one determination was done on each patient and after delivery they were grouped according to the interval of time between the determination of the blood-volume and the date of delivery. All patients were routinely placed on oral iron at the time of their first visit. The blood-volume of 16 healthy non-pregnant women of child-bearing age was used to establish a normal value for the blood-volume in women.

The authors found that there is an initial drop in the total red cell volume of approximately 200 ml. during the first 2 months of pregnancy. This is followed by a progressive rise to a peak in the 9th month, which is 270 ml. above the normal non-pregnant value. The last month before delivery shows a 170 ml. decrease in total red cell volume. At delivery and during the immediate post-partum period there is a further decrease of 300 ml. to a level which is approximately 200 ml. below normal. During the 6 weeks' post-partum period there is a slight but probably statistically significant increase but the level obtained is still 140 ml. below the normal level.

Beginning with the 1st month of pregnancy there is a definite but steady increase in the plasma volume which reaches a peak in the 9th month, approximately 1,200 ml. above the normal value. As with the total red cell volume, there is a significant drop of 190 ml. prior to delivery. In the immediate post-partum period the plasma volume falls another 780 ml. but is still 180 ml. above the normal value. By the end of 6 weeks post-partum the volume is still 100 ml. above normal.

Because the fall in the total red cell volume is greater than the rise in plasma volume in the first 2 months of pregnancy there is a small drop in the whole blood-volume during this period. Following this the rapidly increasing plasma volume is reflected in a rapid climb in the total blood-volume with a maximum increase averaging 1,400 ml. During the last month of pregnancy the total blood-volume drops 350 ml. and immediately after delivery the volume has diminished an additional 1,100 ml. So the total blood-volume immediately post-partum is about the normal level for the non-pregnant woman.

No previous study has pointed out, as do the data presented here, that there is an initial drop in the total red cell volume. This indicates that there is a true anaemia during the first and second trimesters and that the decrease in red blood count and haemoglobin is not entirely due to hydraemia, as has been postulated. The mechanism for the development of this anaemia is not known but it may be due to a decrease in the rate of formation of red cells or a decrease in the life span of the red cell, or a combination of both factors. *John P. Erskine*

243. **A Simple Test of Hormonal Activity by Examination of the Cervical Mucus.** (Un semplice metodo d'esame del muco cervicale nella diagnostica ostetrica e ginecologica.)

By A. MASSANO and S. MONTICELLI. *Minerva Ginec.*, **5**, 368, May 31, 1953. 4 plates. 20 refs.

The cervical canal must be cleared of thick glairy

mucus and a drop of clear liquid secretion obtained by suction in a fine pipette from the cervical canal without admixture with blood. The droplet is allowed to dry on a glass slide when crystallization of its NaCl content occurs, giving characteristic figures depending on the concentration of oestrogen. In good concentration, as on the 10th to 12th days of the menstrual cycle, a liberal crystallization takes place giving rise to figures comparable in form to the fronds of *Felix mas*. During the second half of the cycle, during pregnancy and in cases of marked deficiency of oestrogen no such crystalline forms are obtained. There is, however, a margin of error which makes the test unreliable as a substitute for the established biological tests of early pregnancy, though it can be useful as an aid to the clinical diagnosis of this condition, and also to check the adequacy of therapeutic doses of oestrogen. *W. C. Spackman*

244. **Intrauterine Roentgenography as an Aid in Determining Foetal Age. A Preliminary Report.**

By T. W. Adams, J. M. Whitely, and M. H. Parrott. *West. J. Surg.*, **61**, 448–452, Aug. 1953. 1 fig. 4 refs.

During their work on diabetes and pregnancy (Abstract 254) the authors found that some reliable method of assessing the foetal age was necessary; in particular they wished to know when the foetus had reached 35 weeks. The most reliable index has been found to be the appearance of the distal epiphysis of the femur. This is most easily seen in a lateral film. When the pregnancy was estimated to be about 32 weeks, X-rays were taken weekly until the epiphysis was visible. Pregnancy was then terminated. The procedure was carried out in 15 diabetic women and 80 per cent showed calcification of the epiphysis by the 37th week. There is slight evidence that in some cases the diabetes delays ossification. It is felt that further work on these lines is justified.

*D. C. A. Bevis*

245. **The Effect of Maternal Toxaemia on Foetal Gonadal Activity.**

By F. P. Zuspan. *Amer. J. Obstet. Gynec.*, **66**, 46–53, July 1953. 15 refs. 4 figs.

It has been shown, especially by Smith and Smith of Boston, that gonadotrophic hormone is increased in toxaemic pregnancy. It is therefore a reasonable assumption that the foetal gonads which are normally relatively inactive would show increased activity in toxaemic pregnancy. Govan and Mukherjee (*J. Obstet. Gynaec. Brit. Emp.*, **57**, 525, 1950) reported maturation, cystic atresia and luteinization in the ovaries of foetuses from toxaemic mothers. The present author has compared the gonads born of 32 normal and 8 toxaemic mothers. In the non-toxaemic group 17 of the 32 gonads showed no gonadotrophic stimulation at all; in the remaining 15 the degree of stimulation was minimal or moderate at most. All the gonads in the toxaemic series displayed some degree of stimulation. While this was frequently of a marked degree the severity of the toxaemia could not be correlated with the amount of gonadal change. *F. J. Browne*

246. **Toxemia of Pregnancy and Altered Renal Circulation.**

By B. Wylie. *Amer. J. Obstet. Gynec.*, **66**, 254–268, Aug. 1953. 8 figs. 18 refs.

The author believes that the cause of toxaemia of pregnancy is altered renal circulation due to increased intra-abdominal pressure, compression of the ureters, or any condition such as pyelitis which might cause increased tension in the kidney within its rigid capsule. In the ischaemic kidney a vasoconstrictor substance is produced with resulting hypertension. Oedema is due to diminished glomerular filtration and sodium retention while albuminuria may also be due to the increased intra-abdominal pressure interfering with renal venous drainage. The erect posture whereby the kidney and its vessels and the ureter are compressed is an important contributing factor explaining why toxaemia does not occur in the lower animals and its rarity in primitive peoples, who having no tables or chairs, normally spend much of their time in a semi-quadruped position.

[This is a pretty theory but there are a few difficulties in fully accepting it. Toxaemia and even eclampsia occur in hydatidiform molar pregnancy, sometimes as early as the 17th week and even when the uterus is not much enlarged. Toxaemia is probably not more frequent in pyelitis where there is urinary back pressure and inflammation of the kidney. Moreover, it is doubtful whether in pregnancy the intra-abdominal pressure is increased. Paramore claims that it is, but Theobald, after experimental investigation, denied it, and studies of kidney function have shown that the renal blood-flow in pre-eclampsia is not diminished.] *F. J. Browne*

247. **Habitual Abortion.**

By A. Grant. *Fertil. & Steril.*, **4**, 169–170, Mar.–Apr. 1953.

As a result of work in Sydney the author concludes that 25 per cent of married couples complained of this condition and he advocates preconceptional investigation of the husband and of the uterus especially, as he has found that 53 per cent of the husbands had a high incidence of abnormal spermatozoa. Moreover, premenstrual curettage demonstrated an abnormal endometrial pattern in 55 per cent of the women. Ten per cent of the female patients had a congenital abnormality of the uterus as revealed by hysterogram. He notes that in his series of 109 cases there was no blood group incompatibility or Rhesus factor, and states that in 35 per cent of them thyroid extract was exhibited. Dr. Grant is moderately convinced that the Stilboestrol treatment of America and the Progesterone implant treatment of London are worthy of continuance, though, if abortion is threatened, neither is of any use. It would seem that in Australia the condition of so-called cervical "incompetence" has been recognized and satisfactorily dealt with by plastic operation. *V. B. Green-Armytage*

248. **Habitual Abortion and Pseudosterility.**

By I. Halbrecht. *Fertil. & Steril.*, **4**, 272–284, July-Aug. 1953. 5 figs. 8 refs.

The author is of the opinion that too much emphasis has been put upon hormonal dysfunction and embryonal malformations as a cause of habitual abortion. He thinks that malformations and miscarriages are often caused by unfavourable intra-uterine conditions which influence the development of the trophoblast and result in defective vascularization at the site of the implanted ovum. During the last 10 years he has studied 185 women sent to his clinic in Israel for habitual abortion. Ninety-five of these cases were investigated by hysterography and it is interesting that he discovered malformation of the uterine cavity (uterus bicornis or a uterus arcuatus) in 40 of these, and that the uterine cavity was normal in only 19 patients. Considering what little attention is given to this subject in Great Britain, it is worth noting that, amongst these habitual abortion patients, there were several in whom hysterography revealed a remarkably small cavity and an unusually elongated cervical canal —a condition that he considers is an anomaly of development rather than the result of hormonal disturbance, for in none of them were there deviations from the normal in their endometrial biopsies or basal temperature curves. The author was able to demonstrate intra-uterine adhesions in 26 patients and submucous myomata in 6. It is for these reasons that he advises radiological investigation of all such cases for he considers that intra-uterine environmental conditions play a greater role in the aetiology of female infertility than has hitherto been assumed.

*V. B. Green-Armytage*

249. **Pregnanediol Excretion and Corpus Luteum Therapy in Habitual Abortion.**

By R. ALDER. *Fertil. & Steril.*, **4**, 170–172, Mar.-Apr. 1953.

Ninety women who had had previously 2 or more abortions were investigated. Each woman had weekly pregnanediol tests either till they aborted or carried to the 36th week. He considers that the test is useful and reliable for the control of hormone therapy in habitual abortion. He states that spontaneous abortion occurred in 27 per cent of cases studied, and he recommends that in the treatment of such patients they should have 10 mg. of oral ethesterone daily till the 12th week, and thereafter 20–30 mg. daily until the 36th week, increasing the dose where necessary.

*V. B. Green-Armytage*

250. **Urinary Androgen Levels in Threatened Abortion.** (Risultati del dosaggio degli androgeni urinari in alcuni casi di minaccia di aborto.

By G. BARTOLOMEL. *Riv. Ostet. Ginec. prat.*, **35**, 420–424, Aug. 1953. 14 refs.

The author investigated urinary androgen levels in 27 women with threatened abortion. He used the photometric method of Pincus which he considers selective for 17-ketosteroids. At the same time he estimated the urinary excretion of phenolsteroids and pregnanediol. The women were in the 2nd to 4th month of pregnancy. All were apparently healthy; none showed any sign of virilism.

In none of the women was there any significant rise or fall in the excretion of phenolsteroids and pregnanediol. In 16 women the 17-ketosteroid estimation ranged from 7.1—10.5 mg. per 24 hours; in 11 women this estimation varied from 11—19 mg. per 24 hours.

The author considers that the urinary androgen levels in this last group are well above the normal range (8—10 mg. per 24 hours) for this period of pregnancy. He interprets these results as indicative of a state of hyperandrogenism in a proportion of women with threatened abortion. He speculates at some length on the possible causes of this hypothetical state.

[Examination of the data shows that these 27 women were subsequently treated with oestrogens, progesterone and vitamin E, that 21 went on to have abortions and that 2 of the 6 with continuing pregnancies had a 17-ketosteroid level which the author believed was above the normal limit.] *M. Caturani*

251. **Some Aspects of Anuria in Obstetrics and Gynaecology.**

By J. L. WRIGHT. *N.Z. med. J.*, **52**, 247–257, Aug. 1953. 2 tables. 31 refs.

Anuria and oliguria appear in many ways in obstetrics and gynaecology:

1. Pre-renal, due to diminished intake or to haemorrhage or shock.
2. Renal, due to cortical necrosis, lower nephron nephrosis; and following abortifacient solutions, incompatible blood transfusion, sulphonamide overdosage and nephritis.
3. Post-renal, due to mechanical effects.

The author reviews the recent literature and then gives in detail a regime of treatment based on a modified Borst diet (Bull, Jockes and Lowe, *Lancet*, **2**, 229, 1949). He recommends rigid restriction to 1 litre of fluid plus a volume equal to the urine excreted the previous day. This fluid is a suspension of glucose 400 g., peanut oil 100 g., acacia, and sodium to replace that excreted in the urine. This diet is continued until a diuresis is established, when copious fluids and 20–30 g. of salt are given, if necessary by the intravenous route. The importance of the potassium level in the blood is stressed and the electrocardiographic changes resulting from alterations in the level are given in detail.

Illustrative case histories are given of a fatal case of septic abortion due to *Cl. welchii*, with tubular necrosis, a severe case of vomiting and diarrhoea in pregnancy with potassium depletion; and a case of oliguria following antepartum haemorrhage with severe water depletion.

[This paper is written from the practical viewpoint, and should be of use to one confronted with an unusual case of oliguria.] *L. Woodrow Cox*

252. **Pregnancy and Healed Subacute Bacterial Endocarditis.**

By P. PEDOWITZ and L. M. HELLMAN. *Amer. J. Obstet Gynec.*, **66**, 294–301, Aug. 1953. 10 tables. 20 refs.

This is a review of 120 cases collected by questionnaire or reported in the literature. In the first 6 months after clinical cure of subacute bacterial endocarditis there is great danger of reactivation of the disease should the patient become pregnant, and if she does so therapeutic abortion without tubal ligation is indicated in the first trimester, because of the greatly increased risk of congestive failure. Awareness that the disease may complicate heart disease in pregnancy even in the healed group is the most important factor in diagnosis and it should be suspected in cardiac patients if there is pyrexia, especially if decompensation is present. Intensive antibiotic therapy should be started as soon as the diagnosis is established by positive blood culture.

The authors consider that all patients with heart disease in pregnancy should receive prophylactic antibiotics beginning with the onset of labour and continuing into the puerperium. The best drug is terramycin or aureomycin, 500 mg. being given by mouth every 6 hours from the start of labour. If these are not available penicillin may be used instead.

*F. J. Browne*

253. **Management of the Pregnant Diabetic.**

By M. I. Drury. *J. Irish med. Ass.*, **33**, 91–95, Oct. 1953. 7 refs.

In this article the author reviews a series of 43 pregnancies occurring in 24 diabetic patients under his care. There were no maternal deaths in the series but only 20 babies survived; there were 12 abortions, 6 stillbirths, and 5 neonatal deaths. Drury does not believe that diabetes can ever be considered an indication for termination of pregnancy. In the management of the pregnant diabetic the following measures are considered to be important.

(1) Careful control of the diabetic state.

The patient ought to be examined at fortnightly intervals and careful attention paid to the insulin requirements. Lowering of the renal threshold in pregnancy makes it difficult to assess the insulin requirements and in addition may result in acidosis due to the continuous loss of sugar. The author has had a limited experience in the use of N.P.H. insulin; this preparation contains one third of the amount of protamine sulphate as compared with ordinary protamine zinc insulin. With this form of insulin the author has been able to control more easily the changing insulin requirements in pregnancy.

(2) Induction of labour or Caesarean section at the 36th week.

The advantages and disadvantages of surgical induction of labour and Caesarean section carried out at the 36th week are discussed. Delay in the onset of labour, prolonged labour and intra-uterine infection are considered important disadvantages of surgical induction of labour. Caesarean section at the 36th week has many advantages but for the young Irish mother, with a possible future of repeated pregnancies, there is a natural reticence to perform Caesarean section.

(3) Management of the infant.

Because of the need for specialized paediatric care the author believes that all diabetic women should be delivered in a hospital where every attention can be given to the child. Cyanotic attacks are common in the babies and a number die of respiratory complications. Hypoglycaemia is considered by many paediatricians to be an unimportant cause of neonatal death but the author believes that the infants of some diabetic mothers may be conditioned to a relatively high blood sugar and the rapid fall to a low normal level after birth may have a deleterious result. The following points in management are suggested.

1. Special attention should be paid to ensuring a clear airway.
2. The stomach contents should be aspirated.
3. There should be no feeding during the first 24 hours.
4. An oxygen tent should be used for the first 24 hours.
5. The baby should be given parenteral glucose.

Careful attention ought to be paid to the mother's insulin requirements after delivery; there is a rapid fall in the amount required and unless this is recognized serious hypoglycaemia may result.

In Drury's opinion an improvement in the foetal survival rates could be achieved by education of doctors and patients to the need for close supervision of pregnancy from the earliest weeks. Too many patients reach the last trimester of pregnancy with the diabetic state poorly controlled.

*J. K. Russell*

254. **Diabetes and Pregnancy.**

By J. M. Whitely, T. W. Adams, and M. H. Parrott. *West. J. Surg.*, **61**, 439–447, Aug. 1953. 1 fig. 9 refs.

The authors consider 112 pregnancies from the Good Samaritan Hospital, Portland. Seventy-two reached viability and the foetal mortality was 19 per cent. Thirty-one patients were delivered vaginally (foetal loss 29 per cent) and 41 delivered by Caesarean section (foetal loss 12 per cent). Seventeen cases of toxaemia occurred and 15 cases of hydramnios. The main method of treatment was close teamwork between the physician, obstetrician, and paediatrician; the diabetes was controlled as carefully as possible, delivery effected by Caesarean section as near to the 35th week as possible and the babies given appropriate paediatric care including subcutaneous glucose. Oestrogens were used in too few cases for any conclusions to be drawn. The authors conclude that the main obstetric point is to choose the optimum time of delivery rather than rely on Caesarean section *per se*; they have used a radiological method of assessing foetal age (reported in Abstract 244). The part played by the duration, severity, and control of the diabetes cannot be ignored as there appears to be some correlation between these factors and foetal survival.

[The original paper should be consulted for all the details of this series of cases.]

*D. C. A. Bevis*

255. **Pregnancy and Multiple Sclerosis.**

By W. J. SWEENEY. *Amer. J. Obstet. Gynec.*, **66**, 124–130, July 1953.

This is a report on 22 women with multiple sclerosis complicating pregnancy in the New York Lying-in Hospital since 1932, the incidence being 0.27 per 1,000. Six of the patients were primiparae and 16 multiparae and there were altogether 52 pregnancies. In 13 women the disease had started before any pregnancy. It did not seem to have any adverse effect on the pregnancy, neither was there any evidence that pregnancy had any effect on the ultimate course of the disease. Therefore, termination of the pregnancy because of multiple sclerosis is not indicated.

*F. J. Browne*

256. **Myasthenia Gravis and Pregnancy.**

By D. FRASER and J. W. A. TURNER. *Lancet*, **2**, 417–419, Aug. 29, 1953. 12 refs.

The authors review the literature and quote the experiences of Keynes who found that the myasthenic symptoms were worse premenstrually and during the first 1–2 days of the period and then tended to improve; the effects of pregnancy on the disease were very variable; and there was no indication for the termination of pregnancy.

A review is then made of a series of 14 patients, 7 of whom had already had their pregnancies when first seen so that the authors had to rely on the patient's own account of symptoms during the pregnancy. Of the remaining 7 patients, 6 were delivered in hospital and one in her own home. From their observations they confirm that the effects of pregnancy on myasthenia gravis are very variable and the dosage of neostigmine has to be varied accordingly. One patient had a thymectomy during pregnancy with subsequent improvement. In view of the possibility of premature labour admission 2–3 weeks prior to term is advised. The labour tended to be short, possibly because of the good relaxation. Forceps were needed in 1 case owing to the mother's inability to aid the expulsive powers of the uterus. In the puerperium they found there was a definite possibility of a relapse or exacerbation of the myasthenic symptoms particularly during the first 2–3 weeks. One infant showed definite evidence of myasthenia and there was the possibility that the baby delivered at home also had myasthenic symptoms. This neonatal myasthenia responds to neostigmine and tends to recover in 2–3 weeks.

*H. H. Fouracre Barns*

## LABOUR

257. **Hyperextension of the Foetal Head in Breech Presentation.**

By C. M. DOUGHERTY, L. J. MICKEY, and J. T. MOORE. *Amer. J. Obstet. Gynec.*, **66**, 75–78, July 1953. 6 refs. 2 figs.

A case is described in which this abnormality was present together with hyperextension of the cervical spine so that the face of the foetus was facing upwards. A repeat X-ray 2 weeks later, at the 39th week, showed the position to be unchanged. External manipulation failed to flex the head and Caesarean section was done before the onset of labour. The cause is unknown, though spasm of the neck muscles, uterine abnormalities and tumours have been blamed, but in most cases no cause can be found. It is often noted that the muscles are functionally shortened after the hyperextension has been present for any length of time. In vaginal delivery the risk to the child is much increased, among the accidents reported being transection of the spinal cord, dislocation of the cervical vertebrae, and dislocation of the head of the tibia. The abnormality would doubtless be found more often if X-rays were routine in all breech presentations, and the authors advise this as well as routine inclusion by the radiologist of a statement about flexion, extension or hyperextension of the head. When the head is merely deflexed treatment is expectant and vaginal delivery may be expected, but if it is hyperextended and does not undergo spontaneous correction, Caesarean section should be done before labour starts.

*F. J. Browne*

258. **Rupture of a Corpus Luteum Cyst during Labour.**

By K. NIEMINEVA. *Ann. chir. gynaec. fenn.*, **42**, 109–116, 1953. 13 refs.

This is a case report with a very full discussion, treatment being lower segment Caesarean section with removal of the cyst. Pre-operative diagnosis was not made, section being performed on account of sudden severe abdominal pain in labour associated with foetal distress in a para-3.

*D. M. Sheppard*

259. **Rupture of the Rectovaginal Septum at Parturition.**

By G. F. MELODY. *West. J. Surg.*, **61**, 475–477, Aug. 1953. 2 figs. 6 refs.

A case is reported from the University of California School of Medicine of rupture of the rectovaginal septum without rupture of the perineum. This occurred in a 3rd para who had had a Whitehead-type haemorrhoidectomy in the early puerperium of her last pregnancy. The author considers that the resultant scarring diminished the mobility of the vagina and so caused the peculiar tear. If haemorrhoidectomy is to be performed it should be done during the first trimester or after the puerperium. In repairing the tear the author conserved the anal sphincter, did not mind tying the sutures outside the rectum and confined the bowels postoperatively for one week. The use of neomycin to sterilize the bowel is recommended.

*D. C. A. Bevis*

260. **Post-Partum Haemorrhage.** (Die Nachgeburtsblutung.)

By W. SCHELLENBERG. *Gynaecologia (Basle)*, **136**, 151–164, Sept. 1953. 9 figs.

This is a detailed statistical study of post-partum haemorrhage in 4,562 vaginal deliveries, observed over a period of 5 years. Post-partum haemorrhage was taken to mean a loss of blood after delivery of 500

ml. or more and in this series the incidence was found to be 10.4 per cent.

Two facts emerged from this study. First it was found that there was a definite seasonal incidence which reached its maximum during the month of April with a smaller peak during November.

Secondly it was found that individual midwives varied in the incidence encountered in their cases. Midwives are divided into four groups, based on their training and character. The incidence in the individual midwife varied by as much as 10 per cent, while the incidence in one midwife, as compared with another, varied between 3.5 per cent and 7.9 per cent.

These facts must be taken into consideration in reporting statistics concerning post-partum haemorrhage and in formulating proposals for lowering its incidence.

[This detailed study presents an aspect of the problem of post-partum haemorrhage which has received little attention in the available literature. It serves to emphasize the need for careful training of midwives and students in the management of the third stage, and of devising all possible means to reach a routine which will reduce post-partum haemorrhage to the unavoidable minimum.] *Josephine Barnes*

## PUERPERIUM

261. **Pyrexia in the Puerperium.**

By R. M. CALMAN and J. GIBSON. *Lancet*, **2**, 649–652, Sept. 26, 1953. 8 tables. 11 refs.

This article records the investigation into 954 cases of puerperal pyrexia occurring in 1951 at Queen Charlotte's Hospital. These patients had a temperature of 99.4°F. occurring once during the first 14 days of the puerperium. In 499 patients the pyrexia occurred in the first 24 hours only and was considered to be of no significance. The chief causes of the pyrexia were genital tract infection in 141 patients and urinary infection in 132 patients. The organisms mainly responsible for the genital tract infection were an anaerobic streptococcus in 48 cases, *Staphylococcus aureus* in 23, aerobic non-hemolytic streptococcus in 19 and *Streptococcus viridans* in 11. Sixty-five per cent of the patients with genital tract infections had experienced some obstetrical interference or tissue damage during delivery. In 188 of the pyrexial patients the temperature reached notifiable standard of 100.4°F. The distribution of the causes of the notifiable pyrexia was urinary tract infection 29 per cent, genital tract infection 26 per cent, non-obstetric causes 16 per cent, breast infection 11 per cent, and no cause 17 per cent. The authors suggest that the older practice of notifying cases of uterine infection rather than puerperal pyrexia should be restored. *H. H. Fouracre Barns*

## ANAESTHESIA

262. **Lumbar Epidural Block: The Anaesthetic of Choice for Caesarean Section? A Report of One Hundred Cases.**

By D. C. MOORE, L. D. BRIDENBAUGH, C. K. OWEN, M. P. MACDOUGALL, and H. C. CARRUTHERS. *West. J. Surg.*, **61**, 459–464, Aug. 1953. 6 figs. 2 refs.

The value of regional analgesia for Caesarean section need not be stressed but spinal analgesia frequently results in severe and prolonged headache; epidural block is believed to avoid this. The patient is placed in the lateral decubitus or the sitting position and, after skin preparation, a 19 gauge 3 inch needle introduced under local anaesthesia with its bevel towards the patient's head and advanced ½ to 1 inch until its point is in the interspinous ligament. The level depends on the type of incision planned, 1st lumbar for midlines and 2nd lumbar for Pfannenstiels. A 3 ml. syringe full of anaesthetic solution is attached and steady pressure exerted on the plunger. If injection is easy, the needle lies in the posterior part of the interspinous ligament and the point should be advanced until there is considerable resistance to injection. The needle is slowly advanced while steady unremitting pressure is applied to the plunger. The moment the bevel enters the epidural space a sudden release of pressure occurs and further advance is immediately stopped. Careful aspiration in 4 planes for blood and C.S.F. is made and if none is obtained the remaining solution in the syringe should be injected (1.5—2.0 ml.). The syringe is disconnected and 5 minutes allowed to elapse, the needle being watched for the escape of spinal fluid or blood. If C.S.F. escapes a spinal anaesthetic is given and, if blood, the needle adjusted or a new interspace used. If there is no drainage from the needle, test the abdomen and chest for anaesthesia; if the area is small and the pulse and blood pressure are unchanged it is safe to assume that the dura has not been invaded and a further 9–12 ml. solution given after careful aspiration tests. One half is given with the bevel cephalad and the other half with the bevel caudad. The anaesthetic solution is a mixture of 25 ml. 2 per cent Xylocaine, 50 mg. Pontocaine, and 0.2 ml. adrenalin 1:1000. This is rapidly effective (15–20 minutes) and lasts for 2¼–2¾ hours. The dosage varies between 12 and 15 ml. Premedication consists of 100 mg. Demerol and 1/100 gr. atropine. The contra-indications to epidural block are the same as those for spinal. Vasopressor drugs are not used prophylactically but should be available for immediate use as should also be oxygen. Post-operative nausea and vomiting are controlled by 50 mg. Dramamine i.v.

One hundred cases were treated at the Mason Clinic, Seattle, without severe complications. Four cases had continuous blocks during the post-delivery interval but neck stiffness and headache were troublesome. The only complication was hypotension 15–20 minutes after induction and this responded rapidly to vasopressor drugs given i.v. Anaesthesia extends from T7 to S1. Five cases required Pentothal for control of restlessness. The authors conclude that epidural block has many advantages for Caesarean section.

*D. C. A. Bevis*

263. **The Effects on the Newborn of Pethidine used as an Obstetric Antispasmodic.** (Les effets sur le nouveau-né de la péthidine employée comme antispasmodique obstétrical.)

By P. GUILHEM, A. PONTONNIER, R. BAUX, P. BOURBON, and P. BENNET. *Gynéc. et Obstét.*, **52**, 196–201, 1953. 11 refs.

The writers wished to test the claim of Snoeck and Roemans published in the 1946 report of the 12th Congress of the French Speaking Association of Gynaecologists and Obstetricians regarding the depressing effects of Pethidine on the respiratory centre of the foetus. Their paper is divided into three sections: (1) A comparative statistical clinical study of mothers (and their infants) who had received Pethidine in the course of labour and those who had not. (2) Research into the passage of this product across the placenta. (3) A study of the influence of Pethidine on the oxygenation of the foetus.

(1) *Clinical study.* 525 cases were studied between 1949 and 1951 at the Obstetrical Clinic at Toulouse; one or more ampoules of 100 mg. of Pethidine were given in the course of the confinement.

After excluding, firstly, all confinements where there was any evidence of foetal trauma, and, secondly, where other antispasmodics or anaesthetics had been given, there remained 306 cases.

In order to test the impression of other authors that the ill effects depend upon whether the drug is administered to the mother within 2 hours of delivery, 2 special groups of cases were studied:

(*a*) 115 cases where the Pethidine had been injected more than 2 hours before birth.

Foetal mortality—nil.

Foetal morbidity—9 cases of which 5 were shocked, 3 were cyanosed, 1 born apparently in the act of death.

Making a figure of 7.7 per cent.

(*b*) 191 cases where the Pethidine was injected less than 2 hours before birth.

Foetal mortality—nil.

Foetal morbidity—5 cases of which 3 were shocked, 2 were cyanosed.

Making a figure of 2.6 per cent.

To establish a comparative study the state of the newly-born baby was studied in 500 control cases of normal confinements where no drugs were given to the mother The following were the figures:

Foetal mortality—nil.

Foetal morbidity—17 cases—13 were shocked, 3 were cyanosed, 1 born apparently in the act of death.

Making the figure 3.4 per cent.

The following were their conclusions:

The foetal morbidity in the Pethidine group is comparable to that of the normal control group, if it is remembered that the drug is not injected routinely but essentially for some more or less severe anomaly of uterine action.

The morbidity in the Pethidine series when it is given within 2 hours of birth is less than in the control normal group.

The higher foetal morbidity rate in the group where the drug was injected more than 2 hours prior to birth can be attributed, not to the antispasmodic nature of the drug, but more to the abnormal course of the labours for which it was administered.

(2) *Study of the transplacental passage of Pethidine.* The writers refer to American authors including Lehman and Aitken who proved that Pethidine was excreted by the kidney, and demonstrated its constant passage from mother to child.

Using a spectroscopic technique the authors concluded that if Pethidine is injected more than 2 hours before confinement no trace of it is visible in the cord blood. If Pethidine is given 20–110 minutes before delivery, the cord blood does contain Pethidine (in 2 of these cases Pethidine was not found, probably demonstrating variation in the permeability of the placenta).

This is perfectly in agreement with authors who forbid injecting into the expectant mother any toxic substances which can act on the foetus within 2 hours of delivery.

Against this remains the fact that, according to clinical studies and contrary to the effects of most antispasmodics, Pethidine even when in the blood of the new-born does not upset its vitality.

(3) *Influence of Pethidine on the oxygenation of the foetus.* The umbilical vein was punctured with the needle of a syringe *immediately* after birth and prior to clamping the cord. The quantities of the drug present in the blood taken in this way were estimated according to the method of Philips and Van Slyke. In this series of 12 cases only babies whose mothers had received the drug within 2 hours of delivery were studied.

After eliminating the cases where apparent dystocia may have been the cause of foetal distress, 3 cases only remained for consideration. The saturation of oxygen in the umbilical vein of these averaged 64 per cent which is high compared with an average normal of 50 per cent as quoted by the Americans Walker *et al.*

Without pressing the value of such a small series of cases, the result appears to tally with clinical findings. Finally it is suggested that Pethidine is the drug of choice as an antispasmodic in labour owing to its innocuous effect on the child. *D. Maxwell*

## INFANT

264. **Progress in the Reduction of Neonatal Mortality.**

By S. A. WILE. *Amer. J. Obstet. Gynec.*, **66**, 131–137, July 1953. 7 refs.

Prematurity is still the leading cause of neonatal death. Relatively little is known about its causes though the influence of maternal nutrition, of socio-economic factors and of general hygiene and environment have been stressed. Premature infants who survive the first 4 days will probably continue to do so. The most frequent pathological condition found in the

neonatal period is anoxia. Gentleness in handling the anoxic infant is all important. Mechanical respirators and the use of positive pressure in expanding the alveoli are unphysiological, futile, and dangerous, while the so-called respiratory stimulants have a very limited influence and may be harmful. Inflation of the stomach with oxygen to be absorbed by the gastric mucosa is effective despite apnoea or insufficient respiration.

Direct laryngoscopy and bronchial drainage are seldom indicated and may be injurious, though in the occasional incident, if a highly trained team is available, they may be life saving. Infants delivered by Caesarean section seem to have a disproportionately high incidence of asphyxia and are particularly prone to respiratory difficulties but the cause is not clear though it may be due to aspiration. Frequently these babies have an excessive amount of secretion in the airways and in the stomach which may be vomited or aspirated. In addition to careful cleansing of the air passages, the aspiration of the stomach of all babies born by Caesarean section seems to be of value.

The importance of maternal analgesia and anaesthesia is well recognized and the introduction of allylnormorphine to combat neonatal narcosis may prove of significant value. Any infant who has been exposed to anoxia should be kept in an atmosphere of 50 to 60 per cent oxygen with a humidity of about 80 per cent for 12 to 24 hours or more. Suction equipment should be at hand and used to remove all excessive secretion. It is most important that these infants should be checked at frequent intervals by the nursing personnel. Antibiotics are given routinely to all infants subjected to tracheal catheterization and where there has been early rupture of the membranes. Many anoxic babies develop some oedema and the administration of fluids during the first several days may do more harm than good. Later if the baby cannot be fed they are necessary. Oral feedings are started only after the respiratory distress is relieved.

Perhaps the most frequent cause of death in premature infants is the hyaline membrane which is much more common in prematures and in babies born by Caesarean section. The infant may breathe spontaneously and seem normal at birth but shortly after respiration becomes laboured, and cyanosis develops, the breath sounds gradually get less audible and death usually follows in a few hours. Its incidence seems to be reduced by placing all infants with respiratory distress in an atmosphere of 50 to 60 per cent oxygen with 80 to 90 per cent humidity. Infants with hyaline membrane that survive may develop pneumonia so it is wise to start antibiotics early.

Regarding the infants of diabetic mothers, substitutional hormone therapy of the mother in pregnancy is of doubtful value but the oral administration of glucose may be started soon after birth.

*F. J. Browne*

265. **Perinatal Mortality.** (La mortalité périnatale.)
By W. A. Blanc. *Bull. Féd. Soc. Gynéc. Obstét.*, **5**, 281–286, 1953.

The main points which the author makes are summarized as follows:

1. He reviews existing literature on the causes of infant deaths (viz. perinatal deaths).
2. He bases his paper on 450 postmortem findings.
3. Throughout his paper he emphasizes the importance of anoxia as a cause of perinatal deaths in infants.
4. He states that the present system for the classification of infant deaths (viz. perinatal deaths) is confused.
5. He puts forward a new method, naming this the chronological form of classification of perinatal deaths in infants.
6. He illustrates his method by describing anoxia under the headings:
   (*a*) *In utero.*
   (*b*) During transit.
   (*c*) At the moment of birth, and
   (*d*) As a postnatal event.

[The word " perinatal " is not at present recognized by the Registrar General in Great Britain but is widely used in the U.S.A. and elsewhere and includes death *in utero* in late pregnancy, intra-partum death and neonatal death.] *D. Maxwell*

266. **Hyaline Membrane in the Neonatal Lung.**
By A. E. Claireaux. *Lancet*, **2**, 749–753, Oct. 10, 1953. 7 figs. 11 refs.

The author reviews the histological preparations from the lungs of 810 infants examined postmortem at Queen Charlotte's Maternity Hospital and Hammersmith Hospital from 1948–52. 108 of these infants had a hyaline membrane. They had all died in the neonatal period, 71 (66 per cent) dying in the first 24 hours. In 81 (75 per cent) a hyaline membrane was the sole pathological lesion found. One in every 5 had been delivered by Caesarean section and 4 in every 5 were premature.

A review of the histological findings suggested that the primary factor in the production of a hyaline membrane was aspiration of liquor amnii, the squames in this fluid clumping together and losing their cellular identity to form a membrane lining the air spaces of the lungs. To substantiate this hypothesis, the author obtained fresh samples of liquor amnii and prepared hyaline material by incubation in saline of the centrifuged deposit. By injecting a fine suspension of the hyaline material intratracheally into rats the author was able to reproduce a hyaline membrane in the lungs with associated atelectasis. The author concludes that as a prelude to the formation of the hyaline membrane massive aspiration of liquor amnii occurs *in utero*. While the fluid is largely absorbed into the pulmonary circulation, the deposit left behind in the form of hyalinized squames eventually covers the walls of the alveolar ducts and leads to death by suffocation. *H. H. Fouracre Barns*

267. **Radiography in the Diagnosis of Hyaline Membrane.**
By I. Donald and R. E. Steiner. *Lancet*, **2**, 846–849, Oct. 24, 1953. 12 figs. 5 refs.

The authors have investigated radiographically 28 newborn infants with respiratory distress. They conclude that radiographic shadows in the lungs are sometimes visible when a hyaline membrane is present and represent an associated type of atelectasis. At first there is a fine miliary mottling uniformly distributed throughout the lung fields which probably arises from diffuse alveolar collapse and which appears within a few hours of birth. If the clinical course is downhill this mottling becomes coarse and tends to coalesce. Finally the shadows become confluent and lobar or lobular consolidation and collapse are seen. On the other hand, if the clinical condition improves, the fine mottling resolves and the lung fields become clear. *H. H. Fouracre Barns*

## GYNAECOLOGY

268. **Femoral Retrograde Arteriography in Gynaecological Practice. (Diagnosis of Ectopic Gestation and of Placental Localization.)** (L'artériographie fémorale rétrograde en pratique gynécologique. [Diagnostic de grossesses ectopiques et du localisation du placenta].)

By M. MAYER and J. CHALUT. *Bull. Féd. Soc. Gynéc. Obstét.*, **5**, 312–320, 321–324, 1953. 14 figs.

Radiological investigations by injection of a contrast medium into the vessels of the genital tract can bring an important contribution to the diagnosis in certain circumstances.

Venography constitutes a harmless procedure which has given interesting results in the hands of radiologists and certain gynaecologists; it has, however, one main drawback which is that it only takes into consideration the return circulation, as it does not enter the capillaries. In particular it does not outline at all the circulation in the region of the uterus, tubes or ovaries and there is a risk of missing important anomalies.

It is therefore to aortography that attention is drawn. In 1930 Sahito Kamikawa performed the first retrograde arteriography with a contrast medium, using one of the iliac arteries. Later, Farinas and then Harnett used this procedure in determining by radiological methods the localization of the placenta.

It is only since 1949 that the Swedish writers Borell, Fernström, Lindblom, and Westman (*Acta radiol., Stockh.*, **38**, 247, 1952) thought of the idea of using cutaneous femoral puncture for this purpose. The principle consists in introducing into the femoral artery, using a special technique, a plastic catheter which is pushed up via the external iliac artery, as far as the junction of the common iliac or even just above it.

The importance of passing the catheter up above the junction of the common iliacs is stressed to allow of bilateral views of the pelvic arterial tree being obtained.

Twenty-seven cases are reported, and 15 analysed. The risks in the writers' opinion are minimal and they quote Cournand's statistics who collects 20,000 cases of angiocardiography from 109 hospitals and could only find in the entire world literature 21 deaths.

The technique is described in detail and the following ill effects are listed:

Perifemoral haematoma, a feeling of heat in the pelvis, the sensation of sudden and intense headache, which the writers found did not occur if French fuca of iodine was used.

Fourteen excellent X-ray photographs are shown and these include 3 cases of placentography (in their second paper). *D. Maxwell*

269. **Hormonal Influence on the Uterine Arteries.**

By U. BORELL, I. FERNSTRÖM, and A. WESTMAN. *Acta obstet. gynec. scand.*, **32**, 271–284, 1953. 8 figs. 13 refs.

This is a study of arteriograms of the true pelvis in 62 women, carried out at the Karolinska Hospital, Stockholm. Forty-one of these women were of reproductive age with regular periods (the endometrium, as shown by biopsy, being in the proliferative phase in 20, in the secretory phase in 21), 12 complained of amenorrhoea, and 9 were either at the menopause or post-menopausal. The technique of pelvic arteriography was that described by S. I. Seldinger (*Acta radiol., Stockh.*, **39**, 368, 1953). In cases with regular menstrual periods the width of the uterine arteries was practically identical during the proliferative and secretory phases. The density of the intra-mural branches of the uterine arteries, however, was found to vary greatly during the phases of the menstrual cycle. Between the 10th and 16th day of a 28-day cycle these branches, as demonstrated by arteriography, appeared to be few in number and widely separated, while a comparatively large number was seen throughout the secretory phase, during menstruation and a few days after its cessation. The cause of this apparent paucity of intra-mural blood-vessels around the time of ovulation may be oedema of the uterine wall.

In cases of secondary amenorrhoea the width of the uterine arteries increased under the influence of oestradiol monobenzoate, an increase not shared by any other arteries of the true pelvis. Subsequent progesterone therapy either did not cause any further change or led to a decrease in the calibre of the uterine artery. There was no radiographic evidence to indicate that the width of the uterine arteries bore any relation to the duration of amenorrhoea.

In post-menopausal cases a marked decrease in the calibre of the uterine arteries was noted only in women in whom the menopause had occurred several years ago, and only when associated with a marked decrease in the size of the uterus. *N. Alders*

270. **The Temperature-raising Effect of Female Sex Steroids.** (Die temperatursteigernde Wirkung der weiblichen Sexualsteroide.)

By L. GIANAROLI and G. MOGGIAN. *Gynaecologia (Basle)*, **136**, 129–136, Sept. 1953. 4 figs. 11 refs.

The effects on basal body temperature of female steroid hormones was studied in intact and in castrated rats.

Progesterone was found to have a marked effect in raising basal temperature. This effect was enhanced by previous administration of oestrogenic hormone.

Oestrogenic hormone was found to have a slight temperature-raising effect but much less than that of progesterone.

There is a slight but definite relationship between the dose and the temperature-raising effect.

Castration does not influence the effect of oestrogenic hormone and progesterone in raising body temperature.

These experimental observations are in agreement with the alterations in basal body temperature noted in women during the premenstrual phase of the menstrual cycle and during pregnancy.

*Josephine Barnes*

271. **Experiences with a New Anticoagulant in the Prophylaxis and Treatment of Thrombophlebitis.** (Contributo clinico alla profilassi e terapia delle tromboflebiti con l'impiego di un nuovo anticoagulante.)

By D. CAZZOLA. *Minerva ginec.*, **5**, 465–476, July 31, 1953. 44 refs.

The author describes the use of Tromexan in 30 cases (in obstetrics and gynaecology) exhibiting or threatened with thrombophlebitis. For prophylaxis he recommends a small dose of 100 to 300 mg. daily for a week. In treatment he begins with 600 mg. daily for 1, 2, or 3 days according to the severity of the case, later reducing the dose to 300 and 150 mg. till the symptoms have abated. Total dosage amounted to from 1,200 to 4,800 mg. Tolerance and therapeutic effects are described as excellent. The needs of each case are estimated by the amount of prothrombin in the blood. He advises against the use of antibiotics in such cases as a rule, but advocates the administration of vitamin E.

*W. C. Spackman*

272. **The value of Antibiotics in the Treatment of Female Genital Tuberculosis.**

By A. B. V. RYDÉN. *Acta obstet. gynec., scand.*, **32**, 368–380, 1953. 6 figs. 46 refs.

The author has treated with antibiotics 105 cases of female genital tuberculosis at the Karolinska Hospital, Stockholm, during the past 6 years. These are his recommendations [different in some points from those made by British writers].

(1) In cases of asymptomatic genital tuberculosis neither conservative nor surgical treatment is necessary. In most of these cases the disease does not show any tendency to change its quiescent character. On the other hand, spontaneous healing occurs only rarely. (2) If therapeutic measures are indicated, antibiotic therapy should be given a trial before resorting to surgery. If the disease persists and surgery is necessary, pre-operative treatment with antibiotics facilitates a radical operation technically, and lessens the operative risks and the danger of complications. (3) Streptomycin (0.5 g. twice daily) and isonicotinylhydrazine (0.05 to 0.1 g. 3 times daily) are far superior to P.A.S. (2 g. 5 to 7 times daily) or conteben (0.05 g. daily). (4) P.A.S. or conteben administered at the same time as streptomycin does not increase the antibiotic effect. (5) Streptomycin should be given for at least 2 months, but it is generally unnecessary to continue treatment with this substance for more than 3 months. This should be followed by a 6 months' course of P.A.S. Treatment can then be discontinued provided that there is no evidence of the disease microscopically and bacteriologically. The patient should then attend for follow-up examinations at regular intervals for 2 years after which time the danger of recurrence appears to be small.

*N. Alders*

## STERILITY

273. **One Thousand Cases of Infertility.**

By R. B. WILSON. *Fertil. & Steril.*, **4**, 292–299, July-Aug. 1953.

This is a 5-year review from the Mayo Clinic, and therefore of considerable interest. The author shows that 77 per cent had primary infertility and 23 per cent had secondary infertility. Moreover, 62 per cent of the patients were less than 31 years of age and 57 per cent had been infertile for 5 years or more. Their investigation showed that the cause was in the man in 49 per cent and that only in 7 per cent were both husband and wife found to be at fault. No ascertainable cause of the primary infertility could be found in 42 per cent. He states that all the diagnostic procedures necessary in these cases, including Rubin's test and endometrial biopsy, were completely innocuous, and that iodized oil examinations caused no ill effects or deleterious sequelae. More interesting still is the fact that they have come to the conclusion that the incidence of anovulation (as revealed by regular endometrial biopsies on the 21st–28th day of the cycle) is so infrequent that it can be almost discounted as a cause of infertility where the menstrual history is of the regular pattern. Dr. Wilson does not hold with the opinion that a woman should not be considered infertile until 3 years of marriage have elapsed, and more particularly so if the patient is 30 years of age or more. He goes on to say that a particularly pernicious error on the part of the patient is prolonged use of contraception, for not uncommonly contraception is employed for many years by husbands and wives who are actually or relatively infertile. Moreover, important time is lost for such patients in whom conception is physiologically slow or who may have correctable defects. He therefore urges that contraceptive practices should not be contemplated for periods longer than one year, and particularly for women who marry when they are more than 25 years of age. After stating that in a great number of the infertile patients there is a story of pregnancies which have been illegally interrupted with subsequent cornual occlusion [a thing which we have constantly noted in this country by hysterogram], Dr. Wilson goes on to tell us that a reasonable explanation for absolute or relative infertility can only be discovered in approximately 60 per cent of patients, and that such causes are about equally divided between the two sexes, thus making it essential for a complete study of both parties.

*V. B. Green-Armytage*

274. **Fertility Problems in India.**
By A. STONE. *Fertil. & Steril.*, **4**, 210–217, May-June 1953.

The author was sent by the W.H.O. at the request of the Indian Government to initiate some scheme of family planning, for it is realized in India as well as in Pakistan that an annual increase in the population of 5,000,000 must mean that the population of these two vast areas will double within 50 years. The birth rate was 40 per thousand; whereas the death rate was only 17. At present there are about 50 planning centres, though probably that number should be 5,000. The author considered that the 'rhythm method' of contraception had the greatest advantage, for it was not against tradition and its cost was minimal, though how to instruct the populace was the problem. He considered that a number of coloured beads making a necklace containing 28 beads, one bead for each day of the average cycle was best; orange beads to represent menstruation; green to indicate safety periods, and red for the fertile days. He thought that even the illiterate woman could be instructed to move one bead daily from one string to the other, beginning with the first day of the flow, on the principle of the abacus. One factor against full success at the moment was that at present there is only one physician to every ten thousand of the population in the peninsula.

*V. B. Green-Armytage*

275. **The Male Factor in Fertility and Infertility.**
By J. MACLEOD and R. Z. GOLD. *Fertil. & Steril.*, **4**, 194–209, May-June 1953.

The authors in a long and interesting paper conclude that there are no outstanding changes in spermatozoa production between the ages of 20 and 45, and that as the interval between ejaculations increases the volume and total sperm counts will rise but the percentage of active cells will decrease, justifying an assumption that the age of 40–45 may represent a point at which secondary sex glands begin to show impairment in function. Moreover, there is no question that a high frequency of intercourse depresses the sperm count at all age levels. From their investigations they consider that above the level of 20 million sperms per ml. there is no rise in fertility potential, but that there is a strong relationship between fertility potential and the quality of motility, both of which findings correlate with the fact that there is a progressive decrease in the fertility of the female beginning at about the age of 23. *V. B. Green-Armytage*

276. **Spermigration and Cyclic Changes in Cervical Mucus.**
By P. BERGMAN. *Fertil. & Steril.*, **4**, 183–193, May-June 1953.

The author states that his department in Malmo (Sweden) have discovered that cyclic changes in the cervix are not only in the function of its glands, but also in the physicochemical properties of the mucus. Moreover, the diameter of the cervical canal gradually increases, as does the uterine isthmus, up to the time and completion of the ovulation phase, obviously to favour migration of spermatozoa. All these changes are dependant upon oestrogenic stimulation and are inhibited by progesterone.

He states that during ovulation the cervical mucus is thin and contains a high percentage of water, and that, when the mucus dries, crystals of sodium chloride form into fern-like patterns *in vitro*. This is the optimum time for sperm migration. He contends that sperm migration depends not only upon such cervical conditions but upon the number of spermatozoa in the sperm specimen. *V. B. Green-Armytage*

277. **The Polythene Catheter in Tubal Occlusion.**
By B. RUBIO. *Fertil. & Steril.*, **4**, 233–235, May-June 1953.

Several types of surgery have been attempted to solve the problem of cornual or isthmial occlusion of the tube. Rubin states that 30 per cent of cases of sterility are associated with occlusion of the tubes in some part or other; whereas others like the writer and Stallworthy have discovered by salpingogram that the incidence of occlusion is not more than 10–14 per cent. Hitherto, blockage was most frequently assessed as being due to gonorrhoea but more recent work has shown that isthmial and cornual occlusion is most frequent after septic labour or miscarriage, particularly abortion induced by aretus paste or criminal methods. For occlusion at the cornua silver or tantalum wire, chromic catgut, nylon or ureteric catheters have been used, but recently all of these have been deserted for the use of polythene tubing which is easily sterilized and can be threaded after excision of the blocked portion of the isthmus or reaming out of the interstitial portion of the cornu, through the tube from the fimbria to the vagina. This is an easy technique and the tubing is left in for 4–7 weeks, being removed through the vagina quite painlessly. Dr. Rubio of Mexico City states that 2 of his patients conceived within 3 months of the operation and went to term, and that in 7 patients Rubin's test was postoperatively positive.

[The abstracter has had exactly the same experience and can warmly recommend this technique. Should there be any difficulty in passing the fine tubing down through the uterus, it will be found quite an easy matter to do so if a No. 3 or 4 size polythene tubing is passed first down to the vagina and then through its lumen the finer tubing is threaded.]

*V. B. Green-Armytage*

278. **The Crystallization Test as a Guide to the Treatment of Cervical Hostility.**
By A. CAMPOS DA PAZ. *Fertil. & Steril.*, **4**, 137–148, Mar.-Apr. 1953.

Research has shown that cervical mucus suffers physicochemical modifications during ovulation for the better reception of spermatozoa, and that these changes are stimulated by oestrogens and inhibited by progesterone. In 1950 the above author described a new test for the diagnosis of "cervical hostility" based upon the presence or absence of fern-like crystallization of the cervical mucus at different stages of the cycle. He concludes from work done since then that:

(1) the fern-like pattern is present only in the first half of the menstrual cycle and during the ovulation period. It is absent after ovulation, during pregnancy, and after the menopause. If, however, the menstrual cycle is anovulatory the 'crystallization' effect can be found at any time of the cycle. (2) The fern-like crystallization is closely related to the receptivity of the mucus to spermatozoa, and that when crystallization is absent the mucus is hostile to spermatozoa. The test is easily performed and consists in aspirating the mucus from the endocervix, after cleansing the external os with cotton wool. It is then spread upon a glass slide and allowed to dry over a flame. Under a one hundred magnification the fern-like phenomena can be readily detected by the microscope. Should the crystalline picture be not forthcoming it would indicate that there is a lack of oestrogen and hence would account for infertility due to cervical hostility, indicating a treatment which has proved very satisfactory, namely, giving such a patient a 5 mg. in oil injection of Stilboestrol on the 5th and 10th day of the cycle each month until pregnancy occurs.

*V. B. Green-Armytage*

279. **Endocervicitis.**

By R. GEPPERT and I. F. DAVIS. *Fertil. & Steril.*, **4**, 318–326, July-Aug. 1953. 8 refs.

For many years in many clinics antibiotics have been used parenterally, by mouth, and locally, for cervical conditions including hostility. The authors advise the use of a gelatine capsule of Aureomycin and Stovarsol which is inserted on alternate nights for 2 weeks. They submit a full report of the organisms found in 212 patients and state that 46.7 per cent became pregnant after one or more years of infertility. They consider that it is the antibiotic that reduces the number of organisms and trichomonas in the vagina and permits a 75 per cent improvement in a Sims-Huhner Test. [We have tried penicillin and sulphathiazole vaginal pessaries with similar results where for no obvious reason there has been cervical hostility.]

*V. B. Green-Armytage*

280. **Hormonal Changes Following Low-Dosage Irradiation of Pituitary and Ovaries in Anovulatory Women.**

By A. E. RAKOFF. *Fertil. & Steril.*, **4**, 263–271, July-Aug. 1953. 10 refs.

In America it would appear that there is a far higher proved incidence of anovulation than in this country. The author having taken 40 consecutive patients for treatment gave 20 of them low-dosage irradiation to ovaries and pituitary, and to the other 20, only dosage to the ovaries. He compared these patients with 40 others who were treated solely with endocrines. He found (1) that the clinical and laboratory results in both groups were comparable, improvement in ovarian function occurring in 60 per cent of the first group, and 55 per cent of the second group, with pregnancy resulting in 35 per cent of each group.

(2) That the hormonal studies suggest that low-dosage irradiation increases the sensitivity of the ovaries to the gonadotrophic hormones.

(3) That patients with gonadotrophic deficiency are more likely to improve following low-dosage irradiation than are those with a primary ovarian deficiency. Improvement occurred in 21 of 32 patients of the former group with 13 becoming pregnant, while in the latter group only 2 of 8 improved and 1 became pregnant.

(4) Untoward results occurred in 4 patients, 3 with a gonadotrophic deficiency, and 1 with a primary ovarian deficiency. These effects were temporary in 3 patients and permanent in 1 older patient, aged 41.

*V. B. Green-Armytage*

## NEW GROWTHS OF THE REPRODUCTIVE ORGANS

281. **Investigations on the Diagnosis of Female Genital Cancer by Cervical and Vaginal Smears.** (Recherches sur le diagnostic des cancers génitaux féminins par les frottis cervico-vaginaux.)

By J. VARANGOT, V. NUOVO, and S. VASSY. *Gynéc. et Obstét.*, **52**, 113–153, 1953. 24 figs. 137 refs.

Cytological methods of diagnosis of cervical cancer allow of early discovery of epitheliomas when the cervix presents no appreciable clinical lesion or is masked by an apparently innocent lesion. In these patients presenting repeatedly with suspicious or positive vaginal smears, the best way to demonstrate malignant disease is to carry out conization of the cervix followed by a minute histological study of the fragments removed.

Thanks to this technique it is possible to bring to light the very earliest lesions. The majority of the cancers so revealed are intra-epithelial and are invasive in only a small number of sections.

On the basis of 21 reports of "carcinoma *in situ*" of the uterine cervix the authors discuss the different problems arising. They insist on the necessity of making a conization of the cervix, followed by a study of very numerous sections in order to make the diagnosis.

In 9 cases they found the very earliest beginning of an invasive lesion which had escaped less exhaustive histological studies.

Papanicolaou's technique is the soundest method for discovering "carcinoma *in situ*" which is generally absolutely latent from the clinical point of view or shows itself masked by some apparently innocent cervical lesion. The writers agree that "carcinoma *in situ*" should be classified as Stage 0 in the international classification. They further add that it is undoubtedly true to say that "carcinoma *in situ*" represents the form of onset of invasive cancer but it is not always possible to prove that all intra-epithelial neoplasms finally become invasive.

The most satisfactory treatment in the view of the writers for "carcinoma *in situ*" is total hysterectomy. Amputation of the cervix or diathermy treatment should be reserved only for those patients who are very young.

*D. Maxwell*

282. **Genital Carcinoma in Elderly Women (over 60 years of age).** (Il carcinoma della sfera genitale nelle donne anziane.)

By P. Paracchi and L. Luciani. *Minerva ginec.*, **5**, 355, May 31, 1953. 4 graphs, 5 tables, 13 refs.

This article considers 1,169 cases of carcinoma of the genital organs in women more than 60 years of age treated in the Gynaecological Dept. of the National Cancer Institute of Milan from May 1, 1928, to April 30, 1948. The frequency of carcinoma is found to increase with age and all genital organs are equally involved. Carcinoma of the cervix is the most frequent occurrence, but also the frequency of vulva and corpus uteri carcinomas is noted. The malignant lesions of the genital organs were found to have a slower and less invasive development in old women, and generally the prognosis of these cancers is not less favourable than in younger women. In the cases of carcinoma of the vulva and ovary, however, the results were less successful than in younger women. As regards prophylaxis, any measures to combat the senile dystrophies, whether by operative or therapeutic procedures, or by the removal of useless ovaries when intra-abdominal measures are being taken should bring their reward. *W. C. Spackman*

283. **A Case of Diffuse Carcinosarcoma of the Uterus.** (Carcinosarcoma diffuso del corpo dell' utero.)

By C. Mossetti. *Minerva ginec.*, **5**, 316–320, May 15, 1953. 3 figs. 16 refs.

A case of this rare tumour is reported and discussed in detail, a special point being made that this designation should only be applied to tumours in which the carcinomatous and sarcomatous elements are intimately mixed. These tumours can derive in one of three ways: (*a*) by 'collision' of two tumours. (*b*) by a 'combination' of both carcinomatous and sarcomatous tissue of embryonic type, and (*c*) by malignant transformation of the stromal and epithelial elements of a normal tissue. It is not regarded as possible that the transformation of one element into the other can take place, though such an appearance can be simulated by inflammatory changes in a carcinoma, or even by the effects of radium.

In the case reported, the carcinoma component is represented by a mature type of adenocarcinoma, whilst intimately mixed with it is a typical small round-celled sarcoma, and it does not appear to the author possible to say which of the two malignant elements preceded the other, but it seems to be derived under method (*c*) above.

*W. C. Spackman*

284. **Cases of Myoma of the Vaginal Portion of the Cervix treated at the Helsinki Women's Clinic in 1930–1952.**

By A. Alha and A Pohjala. *Ann. chir gynaec. fenn.*, **42**, 92–100, 1953. 13 refs.

Fifteen cases of fibroids growing from the vaginal portion of the cervix are described briefly. Their frequency of occurrence was 0.21 per cent of all cases of fibroids. Thirteen of the cases were aged between 32 and 50, and 11 were multiparous. Abortion had occurred in 5 cases. Symptoms and differential diagnosis are discussed, the initial diagnosis in 8 cases being prolapse. Treatment was by enucleation, extirpation or total hysterectomy. *D. M. Sheppard*

285. **Carcinoma of the Cervical Stump.**

By V. Tortula. *Ann. chir. gynaec. fenn.*, **42**, 101–108, 1953. 17 refs.

This article is based on observations of 44 cases of carcinoma of the cervical stump following subtotal hysterectomy treated in the Helsinki radiotherapy clinic. The frequency of occurrence of stump carcinoma out of all cases of carcinoma of the cervix treated at the Radiotherapy Clinic was 2.18 per cent. In cases where at least a year has elapsed from the original operation to the onset of symptoms, thus eliminating any carcinomata present but undiagnosed before operation, the incidence was 1.5 per cent. Sixty-four per cent were over the age of 50. In 85 per cent there was a 4-year interval between operation and onset of symptoms. On diagnosis 25 per cent were in Stage I, 32 per cent in Stage II, 29 per cent in Stage III, and 14 per cent in Stage IV. Eighteen cases were treated by radium in vaginal applicators only and 23 cases had radium introduced into the cervical canal in addition. The average dose was: vaginal 5,411 mg. hrs., cervical 1,670 mg. hrs., combined 5,927 mg. hrs. Deep X-rays up to 3,000–4,000 r was also given. Seventeen of the cases have been observed a period of 5 years from the onset of symptoms, and of these only 4 remained symptom free. The treatment is thus disappointing but depends on the amount of radium that can be inserted into the cervical canal.

*D. M. Sheppard*

286. **The Diagnosis of Ovarian Cancer. Results of the Study of 210 Patients by the Philadelphia Committee for the Study of Pelvic Cancer.**

By L. J. Golub. *Amer. J. Obstet. Gynec.*, **66**, 169–177, July 1953. 7 refs. 1 fig. 8 tables.

This 5-year study showed that 9.5 per cent of the 2,219 cases of pelvic cancer were ovarian. Of the 210 patients 18.5 per cent were between the ages of 11 and 40 years, and 21 per cent were over 60.

The most frequent presenting symptoms were abdominal pain, present in 23 per cent, abnormal uterine bleeding in 22 per cent, gastro-intestinal symptoms (loss of appetite, dyspepsia, nausea and vomiting, or rectal pain) 9.5 per cent, and abdominal enlargement 35 per cent.

Every abdominal examination should include a search for free fluid in the peritoneal cavity since ascites may be the first sign of ovarian malignancy. If necessary for accurate diagnosis it is wiser to evacuate the fluid through a small incision under local anaesthesia rather than by a trocar which may puncture a malignant cyst and so spread the disease. Following paracentesis the abdominal, pelvic, and rectal examinations will be much facilitated. The importance of a careful rectal examination in virgins cannot be

over-emphasized. Cytological examination of the ascitic fluid should always be done but though paracentesis was performed many times malignant cells were reported only 4 times in the ascitic fluid. Of the 210 cases, 50 were inoperable. The importance of making an accurate diagnosis of ovarian cancer at the time of operation has not been properly emphasized. This involves the co-operation of the pathologist and the use of frozen sections in order that the surgeon may know how extensive his extirpation should be, and avoid the necessity for a second operation. In this series there were 51 such cases. Physician delay in diagnosis occurred in 17 per cent of the 210 cases and resulted either from failure to make the essential pelvic, rectal, and speculum examinations or from failure to account for the patients' symptoms especially when they were gastro-intestinal.

*F. J. Browne*

## OPERATIONS

287. **Concerning the Electro-coagulation of the Uterine Cervix. A Colposcopy Study of 110 Cases.** (A propos de l'électrocoagulation du col utérin. Etude colposcopique de 110 cas, sous-mis à l'électrocoagulation.)

By J. Berger. *Gynéc. et Obstét.*, **52**, 214–225, 1953. 5 figs. 33 refs.

There are two methods of using high frequency currents, monopolar and bipolar; the former gives a feeble and superficial coagulation; the latter bipolar, is used in a mono or biactive manner.

By *bipolar monoactive coagulation* the writer means that the negative electrode is usually a large lead plaque attached to the bare skin of the patient while the positive electrode concentrates the diathermizing electric paths at one small point of coagulation which, however, can penetrate deeply. By *bipolar biactive coagulation* the writer signifies that both positive and negative poles are applied at the coagulation site; this type extends over the surface and penetrates little by little into the depth of the tissues.

The intensity of the current and the duration of the application can be varied in each case.

*Macroscopically* the intense red colour of the cervix changes and takes on a pale grey opalescent change. At the point of application of the electrode small black points appear. In the course of the first few days congestive signs appear in the periphery of the coagulated zone. Later the congested area becomes bright red and the necrosed tissue begins to separate.

*With the colposcope*, the coagulated zone becomes white and irregular, with a number of black points; 5–8 days later the cervix becomes very congested. The bright red colour of the peripheral tissue contrasts greatly with the opaque, white, treated area. Two weeks later, eroded areas are seen which at the edge are covered by very thin transparent layers of squamous epithelium and 6–8 weeks later, if the coagulation has been satisfactory, the cervix should assume a normal appearance—that is, squamous epithelium which often shows lines concentric with the external os, and the absence of any glands or Nabothian follicles. The presence of regenerated squamous epithelium renders Schiller's reaction negative.

*Microscopically*, the writer agrees with the description by Dryen and Feldmann, who noted that the cells at the site of coagulation are quite unrecognizable. Beneath this layer, destruction and displacement of certain cells are obvious and due probably to the effect of the current. A hyperaemic stage comes first, followed by fibro-leucocytic infiltration in an oedematous tissue about 8 days later.

Between the 8th and 14th days granulation tissue forms surrounded by round cells and fibroblasts. Towards the 4th week, the granulomatous reaction becomes less and regeneration of squamous cells has already started to take place.

In comparing the results of electro-coagulation of diseased cervices the writer concludes that bipolar monoactive methods are better than bipolar biactive. The writers add that the decision to treat the cases was always made on macroscopic evidence which in his opinion is insufficient.

He reports 17 complete successes out of 80 when there was early regeneration and covering of the vaginal cervix with squamous epithelium.

As regards 110 cases of simple leucorrhoea: 40 per cent were cured, 35 per cent were improved, and 25 per cent showed no change.

They further add that the majority of cases of cervical lesions cannot be diagnosed accurately with the naked eye. A plea is made for:

1. Smears from the posterior fornix, vaginal and endocervix.
2. At least one Schiller's test.
3. If possible colposcopy.
4. If necessary a biopsy.

*D. Maxwell*

288. **Hysterography: Accidental injection of Pelvic Veins and Lymphatics.** (Considerazioni sulle iniezioni vascolari in corso di isterosalpingografia.)

By A. Tetti. *Minerva ginec.*, **5**, 439–447, July 15, 1953. 7 figs. 31 refs.

The contrast media used in testing the patency of the Fallopian tubes and in other similar procedures can penetrate into the veins and lymphatics of the female pelvic organs under certain circumstances. This accident occurred in 1.6 per cent of the author's cases of hysterosalpingography. Conditions which favour this complication are hypoplasia, malformation or malposition of the uterus, interstitial closure of the tubes, and injury to the endometrium by the end of the cannula. Excessive pressure and an excessive amount of the injected media no doubt also contribute but are less important than one might expect.

When the contrast media enter the uterine veins the resulting emboli can readily be seen outlining the veins on the X-ray screen but as a rule they do not appear to cause the serious symptoms one might look for, although a few fatal cases have been recorded. Usually the symptoms (syncope, haemoptysis, etc.) are quite mild and of short duration, and they may often pass unnoticed.

The media often penetrate the lymphatics also. This is of no importance though it can easily be diagnosed on the screen where it is of course much longer-lasting than the emboli in the veins.

The author gives details of 8 cases with their X-ray plates. In 4 the lymphatics of the uterus were injected, in 1 those of the uterus and the tubes; in 1 case the lymphatics and the veins of the uterus showed penetration, whilst in 2 cases an almost complete visualization of the uterine veins was obtained.

*W. C. Spackman*

## UROLOGY

289. **Experimental Studies on the Functioning of the Female Urinary Bladder and Urethra.**

By S. KARLSON. *Acta obstet. gynec. scand.*, **32**, 285–307. 9 figs. 11 refs.

These studies were made possible by an ingenious electric recording method which allows a simultaneous graphic recording of the sequence of events in the urinary bladder, the lisso-sphincter and the rhabdo-sphincter to be made.

(1) When fluid is slowly instilled into the bladder the intra-vesical pressure rises almost at once, and at the same time the 2 sphincters begin to contract. (2) Instillation of urine into the proximal part of the urethra produces an urge to micturate, and at the same time contractions in the muscles of the bladder and the sphincters. (3) During voluntary micturition the lisso-sphincters relax first, followed by relaxation of the rhabdo-sphincter, and then rhythmic contractions of the muscles of the bladder set in. (4) During involuntary micturition, evoked by introducing urine into the proximal part of the urethra when the bladder was full, the contractions always followed the same pattern, namely relaxation of the lisso-sphincter, then of the rhabdo-sphincter, and finally detrusor contractions. (5) When micturition is voluntarily interrupted the rhabdo-sphincter, which is under the influence of volition, is the first to contract, but subsequently the lisso-sphincter becomes involved. Micturition is interrupted by this constriction of the urethra. The urine is probably pressed out of the urethra, so that the stimulation from the proximal part of the urethra ceases. (6) The voluntary control over the smooth muscles of the bladder and the lisso-sphincter during voluntary micturition is explained as follows: through an act of volition the muscles of the pelvic floor relax and bring about a lowering of the neck of the bladder. This opens the internal orifice of the urethra. Urine enters the urethra and causes a local excitation on the one hand, and reflexly an increase in excitability of the muscles of the bladder on the other hand. By reciprocal action between the excitation from the bladder and the excitation from the urethra an increase in the tone and contractions of the muscles of the bladder and the urethra is produced first. Secondly, the excitability having exceeded a certain limit, a relaxation of the lisso-sphincter occurs, followed by relaxation of the rhabdo-sphincter and, finally, by detrusor contractions and passing of urine.

*N. Alders*

*For the prevention and treatment of*

*post-partum haemorrhage*

# NEO-FEMERGIN

Neo-Femergin is an association of ergometrine tartrate and ergotamine tartrate, presented in the form of tablets, oral solution and ampoules for intravenous or intramuscular injection.

Neo-Femergin combines the rapid but transient effect on the uterus produced by ergometrine with the prolonged action of ergotamine.

**TABLETS** **AMPOULES**

**ORAL SOLUTION**

*Literature and samples available on request*

**SANDOZ PRODUCTS LIMITED**

134, *Wigmore Street,* *London, W.1*

*Made in Great Britain. Printed by John Sherratt and Son, Park Road, Altrincham*

# THE JOURNAL OF OBSTETRICS AND GYNAECOLOGY OF THE BRITISH EMPIRE

Vol. LX DECEMBER 1953 No. 6

## CONTENTS

PAGE

TOXOPLASMOSIS AND PREGNANCY. *Svante C:son Holmdahl, M.D.* ... ... ... ... 765
PATERNAL INFLUENCE IN POLYZYGOTIC BIRTHS. *A G. Oettle* ... ... ... ... ... 775
HYPERGLYCAEMIA AND HAEMORRHAGIC SHOCK IN PREGNANCY: Preliminary Study ... ... 785
*Robin Murdoch, M.B., M.R.C.O.G.*
LATE EFFECTS OF EARLY AMBULATION IN OBSTETRICS ... ... ... ... ... 793
*H. B. Allee, J. A. Perlin, and Jean A. Peabody*
ENDOMETRIOSIS OF THE PLEURA AND OVARIES ... ... ... ... ... ... ... 823
*Josephine Barnes, M.A., D.M., M.R.C.P., F.R.C.S., F.R.C.O.G.*
THE DIAPHRAGM IN THE PUERPERIUM ... ... ... ... ... ... ... ... 825
*R. Grenville-Mathers, M.A., M.D., M.R.C.P.E., F.R.F.P.S., and H. J. Trenchard, M.B., M.R.C.P., D.M.R.D.*
THE INFANTS OF DIABETIC MOTHERS: A Morphological Study ... ... ... ... 834
*B. S. Cardell, M.D.*
THE POSITION OF THE FOETUS IN RELATION TO PLACENTAL SITE ... ... ... ... 854
*A. S. Whitehead, M.D., M.Rad., D.M.R.D.*
EVOLUTION OF ENDOMETRIAL CARCINOMA STUDIED BY SEQUENTIAL CURETTINGS ... ... 859
*M. David Orrahood, M.D., and John P. Wyatt, M.D.*
TRANSPLANTATION OF THE OVARY INTO THE UTERINE CAVITY FOR THE TREATMENT OF STERILITY IN WOMEN. *P. G. Preston, M.B., Ch.B., F.R.C.O.G.* ... ... ... 862
A CASE OF THE STEIN-LEVENTHAL SYNDROME ASSOCIATED WITH CARCINOMA OF THE ENDOMETRIUM ... ... ... ... ... ... ... ... ... ... 865
*R. D. de Vere, F.R.C.S., M.R.C.O.G., and K. R. Dempster, M.B., B.S.*
PREGNANCY AND POLYCYSTIC DISEASE OF THE KIDNEYS ... ... ... ... ... 868
*W. Gordon Millar, M.B., M.R.C.O.G.*
A STUDY OF EFFECTS OF X-RAYS ON THE GRANDCHILDREN OF WOMEN WHO HAVE BEEN IRRADIATED FOR THE TREATMENT OF FEMALE STERILITY ... ... ... ... 872
*Ira I. Kaplan, B.Sc., M.D., F.A.C.R.*
OBSERVATIONS ON THE COMPOSITION OF THE TOTAL LEUCOCYTE COUNTS DURING THE HUMAN MENSTRUAL CYCLE. *I. L. MacKinnon, M.B., Ch.B.* ... ... ... 878
THE MINOR DEGREE OF HYDROCEPHALUS AS AN OBSTETRICAL PROBLEM ... ... ... 888
*T. Francis Redman, M.B., F.R.C.S.E., M.R.C.O.G., and G. R. Airth, M.B., D.M.R.(D.)*
THE UTILIZATION OF RADIO-IODINE DURING PREGNANCY ... ... ... ... ... 892
*M. J. D. Noble, M.B., F.R.C.S.Ed., M.R.C.O.G., and S. Rowlands, B.Sc., Ph.D., F.Inst.P.*
PLACENTAL METASTASES FROM A BRONCHIAL CARCINOMA ... ... ... ... ... 895
*James S. Barr, M.B., M.R.C.O.G.*
CARCINOMA OF THE UTERINE BODY TREATED WITH RADIOACTIVE COBALT ... ... 898
*Paul Strickland, M.B., M.R.C.P., D.M.R., F.F.R.*
THE COMPARISON OF THE PERINATAL MORTALITY RATES FOR A MATERNITY HOSPITAL 901
*John Thomson, M.D., D.P.H., D.C.H.*
MULTIPLE PRIMARY CARCINOMATA OF UTERUS ... ... ... ... ... ... 904
*Mostyn P. Embrey, B.Sc., M.D., F.R.C.S., M.R.C.O.G.*
THE AETIOLOGY OF ANENCEPHALY ... ... ... ... ... ... ... ... 907
*H. Vincent Corbett, M.Sc., M.D., F.R.C.S., M.R.C.O.G., M.M.S.A.*
SPONDYLOLISTHESIS AND PREGNANCY. *Charles J. Champ, M.D., M.R.C.O.G.* ... ... 913
KRUKENBERG TUMOUR OF THE OVARIES COMPLICATING PREGNANCY ... ... ... 915
*S. Burke, M.D., F.R.C.S., D.Obst.R.C.O.G.*
A CASE OF GRANULAR CELL MYOBLASTOMA OF THE VULVA ... ... ... ... 917
*H. B. Watson, M.B., F.R.F.P.S., M.R.C.O.G., and C. W. Taylor, M.B., Ch.B.*
AN UNUSUAL CASE OF SECONDARY POSTPARTUM HAEMORRHAGE NECESSITATING HYSTERECTOMY. *J. K. Russell, M.B., M.R.C.O.G.* ... ... ... ... ... 919
MONO-AMNIOTIC TWIN PREGNANCY. *John Henderson, M.B., M.R.C.O.G.* ... ... ... 921
AMELIA: Review of the Literature and Report of a Case ... ... ... ... ... 922
*L. O. S. Poidevin, M.B., B.S., M.R.C.O.G.*
OBITUARIES ... ... ... ... ... ... ... ... ... ... 926, 929, 930
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS. NICHOLS FELLOWSHIP ... 932
REPORTS OF SOCIETIES ... ... ... ... ... ... ... ... ... ... ... 933
BOOK REVIEWS ... ... ... ... ... ... ... ... ... ... ... ... 946
REVIEWS OF CURRENT LITERATURE ... ... ... ... ... ... ... ... 951